

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

5 The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1\_1, EZRI\_BOVIN, GGU19889\_1, CC3\_YEAST, S74244, NALS\_MOUSE, MOES\_PIG, S28660, S44860 and YNA4\_CAEEL.

#### EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

20 DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

25 The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH\_1, GIBMUC1A\_1, P\_R96298, AF001406\_1, PVU88874\_1, P\_R85151, AF041409\_1, CELC50F2\_7, C45875, and AB009510\_21.

35 Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.



**EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYP0\_HUMAN, AF049498\_1, GEN14531, P\_W14146, HS46KDA\_1, CINB\_RAT, OX2G\_RAT, D87018\_1, and D86996\_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

**EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

in Example 1 above. This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

5 forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395).

reverse PCR primer 5'-CAGGGACACACTCTACCATTTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

10 5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

15 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34\_BRELC, SP96\_DICDI, S36326, SSU51197\_10, MUC1\_XENLA, TCU32448\_1 and AF000409\_1.

#### EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

35 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing

homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

5 In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

10 The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned  
15 ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff  
20 sequences: MGNENDOBX\_1, CELF41G3\_9, AMPG\_STRLI, HSBBOVHERL\_2, LEEXTEN10\_1, AF029958\_1 and P\_W04957.

#### EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70  
30 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased  
35 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1\_YEAST, AF041382\_1, MAOM\_SOLTU, SPPBPHU9\_1, I41024, EPCPLCFail\_1, HSPLEC\_1, YKL4\_CAEEL, A44643, TGU65922\_1.

#### EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAAGTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

hybridization probe

5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure 288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of

the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298\_1, TETN\_CARSP, TETN\_HUMAN, MABA\_RAT, S34198, P\_W13144, MACMBPA\_1, A46274, PSPD\_RAT AND P\_R32188.

#### 10 EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a  
15 proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle,  
20 Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

25 The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of  
30 approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA\_THETH, GEN11167, MTV044\_4, AB011151\_1, RLJA2750\_3, SNEIPTRA\_1, S63624, C28391, A37907, and  
35 S14064.

Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

**EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P\_W07607, AB000545\_1, AB000546\_1, A1AT\_RAT, AB015164\_1, P\_P50021, COTR\_CAVPO, and HAMHPP\_1. The variants claimed in this application exclude these sequences.

**EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

5 The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned  
10 ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486\_1, AF044205\_1, P\_W31186, CELK03C7\_1, F69034, EF1A\_METVA, AF024540\_1, SSU90353\_1,  
15 MRSP\_STAAU and P\_R97680.

#### EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety  
20 of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a  
25 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
30 The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71.  
35 Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about

amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699\_1, S49589, FIBA\_PARPA, FIBB\_HUMAN, P\_R47189, AF004326\_1, DRTENASCN\_1, AF004327\_1, P\_W01411 and FIBG\_BOVIN.

**EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open-reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1\_YEAST, BPU43599\_1, YS8A\_CAEEL, S67570, LSU54556\_2, S70305, VGLX\_HSVEB, and D88733\_1.



EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198\_5, CELR12C12\_5, S73465, Y011\_MYCPN, S64538\_1, P\_P8150, MUVSHPO10\_1, VSH\_MUMPL and CVU59751\_5.

EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8\_1, LMNACHRA1\_1, HXD9\_HUMAN, CHKCMLF\_1, HS5PP34\_2, DMDRING\_1, A37107\_1, MMLUNGENE\_1, PUM\_DROME and DMU25117\_1.

#### EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence

of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid 379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P\_W36955, MYP0\_HETFR, HS46KDA\_1, AF049498\_1, MYO0\_HUMAN, AF030454\_1, A53268, SHPTCRA\_1, P\_W14146 and GEN12838.

#### EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGCAGCCCCTGTGACACAACTGG-3' (SEQ ID NO:425)

reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II

transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819\_1, HSAJ1687\_1, AF009511\_1, AB010710\_1, GEN13595, HSAJ673\_1, GEN13961, AB005900\_1, LECH\_CHICK, AF021349\_1, and NK13\_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 140: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., *Gene*, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., *supra*. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate•2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO<sub>4</sub>) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

*E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column

using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10  $\mu$ g pRK5-PRO DNA is mixed with about 1  $\mu$ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500  $\mu$ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M  $\text{CaCl}_2$ . To this mixture is added, dropwise, 500  $\mu$ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM  $\text{NaPO}_4$ , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200  $\mu$ Ci/ml  $^{35}\text{S}$ -cysteine and 200  $\mu$ Ci/ml  $^{35}\text{S}$ -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompanyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to

maximal density in a spinner flask and 700  $\mu$ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5  $\mu$ g/ml bovine insulin and 0.1  $\mu$ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as  $\text{CaPO}_4$  or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as  $^{35}\text{S}$ -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by  $\text{Ni}^{2+}$ -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect<sup>®</sup> (Quiagen), Dosper<sup>®</sup> or Eugene<sup>®</sup> (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately  $3 \times 10^7$  cells are frozen

in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2  $\mu$ m filtered PS20 with 5% 0.2  $\mu$ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with  $3 \times 10^5$  cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at  $1.2 \times 10^6$  cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22  $\mu$ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275  $\mu$ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding



PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 µm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound

protein. After reaching  $A_{280}$  baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with  $Ni^{2+}$ -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

#### EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the

art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

5 Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's  
10 instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal  
15 sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high  
20 concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 146: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed  
25 in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO  
30 polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent  
35 and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is

separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

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#### EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced

peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

EXAMPLE 148: Stimulation of Heart Neonatal Hypertrophy (Assay 1)

This assay is designed to measure the ability of PRO polypeptides to stimulate hypertrophy of neonatal heart. PRO polypeptides testing positive in this assay are expected to be useful for the therapeutic treatment of various cardiac insufficiency disorders.

Cardiac myocytes from 1-day old Harlan Sprague Dawley rats were obtained. Cells ( $180 \mu\text{l}$  at  $7.5 \times 10^4/\text{ml}$ , serum  $<0.1\%$ , freshly isolated) are added on day 1 to 96-well plates previously coated with DMEM/F12 + 4% FCS. Test samples containing the test PRO polypeptide or growth medium only (negative control) ( $20 \mu\text{l}/\text{well}$ ) are added directly to the wells on day 1. PGF ( $20 \mu\text{l}/\text{well}$ ) is then added on day 2 at final concentration of  $10^{-6}$  M. The cells are then stained on day 4 and visually scored on day 5, wherein cells showing no increase in size as compared to negative controls are scored 0.0, cells showing a small to moderate increase in size as compared to negative controls are scored 1.0 and cells showing a large increase in size as compared to negative controls are scored 2.0. A positive result in the assay is a score of 1.0 or greater.

The following polypeptides tested positive in this assay: PRO1312.

EXAMPLE 149: Stimulation of Endothelial Cell Proliferation (Assay 8)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus VEGF (5 ng/ml); and (4) ACE cells plus FGF (5 ng/ml). The control or test sample, (in 100 microliter volumes), was then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at  $37^\circ\text{C}/5\% \text{CO}_2$ . After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at  $37^\circ\text{C}$ , the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of a PRO polypeptide was calculated as the fold increase in proliferation (as determined by the acid phosphatase activity, OD 405 nm) relative to (1) cell only background, and (2) relative to maximum stimulation by VEGF. VEGF (at 3-10 ng/ml) and FGF (at 1-5 ng/ml) were employed as an activity reference for maximum stimulation. Results of the assay were considered "positive" if the observed stimulation was  $\geq$  50% increase over background. VEGF (5 ng/ml) control at 1% dilution gave 1.24 fold stimulation; FGF (5 ng/ml) control at 1% dilution gave 1.46 fold stimulation.

The following PRO polypeptides tested positive in this assay: PRO1154 and PRO1186.

EXAMPLE 150: Inhibition of Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)

The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Polypeptides testing positive in this assay are useful for inhibiting endothelial cell growth in mammals where such an effect would be beneficial, e.g., for inhibiting tumor growth.

Specifically, bovine adrenal cortical capillary endothelial cells (ACE) (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus 5 ng/ml FGF; (4) ACE cells plus 3 ng/ml VEGF; (5) ACE cells plus 3 ng/ml VEGF plus 1 ng/ml TGF-beta; and (6) ACE cells plus 3 ng/ml VEGF plus 5 ng/ml LIF. The test samples, poly-his tagged PRO polypeptides (in 100 microliter volumes), were then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO<sub>2</sub>. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of PRO polypeptides was calculated as the percent inhibition of VEGF (3 ng/ml) stimulated proliferation (as determined by measuring acid phosphatase activity at OD 405 nm) relative to the cells without stimulation. TGF-beta was employed as an activity reference at 1 ng/ml, since TGF-beta blocks 70-90% of VEGF-stimulated ACE cell proliferation. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis. Numerical values (relative inhibition) are determined by calculating the percent inhibition of VEGF stimulated proliferation by the PRO polypeptides relative to cells without stimulation and then dividing that percentage into the percent inhibition obtained by TGF- $\beta$  at 1 ng/ml which is known to block 70-90% of VEGF stimulated cell proliferation. The results are considered positive if the PRO polypeptide exhibits 30% or greater inhibition of VEGF stimulation of endothelial cell growth (relative inhibition 30% or greater).

The following polypeptide tested positive in this assay: PRO812.

EXAMPLE 151: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50 :1 of irradiated stimulator cells, and

50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10<sup>7</sup> cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO826, PRO1068, PRO1184, PRO1346 and PRO1375.

EXAMPLE 152: Retinal Neuron Survival (Assay 52)

This example demonstrates that certain PRO polypeptides have efficacy in enhancing the survival of retinal neuron cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at postnatal day 7 (mixed population: glia and retinal neuronal types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N<sub>2</sub> and with or without the specific test PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are stained with calcein AM then fixed using 4% paraformaldehyde and stained with DAPI for determination of total cell count. The total cells (fluorescent) are quantified at 20X objective magnification using CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The effect of various concentration of PRO polypeptides are reported herein where percent survival is calculated by dividing the total number of calcein AM positive cells at 2-3 days in culture by the total number of DAPI-labeled cells at 2-3 days in culture. Anything above 30% survival is considered positive.

The following PRO polypeptides tested positive in this assay using polypeptide concentrations within the range of 0.01% to 1.0% in the assay: PRO828, PRO826, PRO1068 and PRO1132.

**EXAMPLE 153: Rod Photoreceptor Cell Survival (Assay 56)**

This assay shows that certain polypeptides of the invention act to enhance the survival/proliferation of rod photoreceptor cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at 7 day postnatal (mixed population: glia and retinal neuronal cell types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N<sub>2</sub>. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are fixed using 4% paraformaldehyde, and then stained using CellTracker Green CMFDA. Rho 4D2 (ascites or IgG 1:100), a monoclonal antibody directed towards the visual pigment rhodopsin is used to detect rod photoreceptor cells by indirect immunofluorescence. The results are calculated as % survival: total number of calcein.- rhodopsin positive cells at 2-3 days in culture, divided by the total number of rhodopsin positive cells at time 2-3 days in culture. The total cells (fluorescent) are quantified at 20x objective magnification using a CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The following polypeptides tested positive in this assay: PRO536, PRO943, PRO828, PRO826, PRO1068 and PRO1132.



EXAMPLE 154: Induction of c-fos in Endothelial Cells (Assay 34)

This assay is designed to determine whether PRO polypeptides show the ability to induce c-fos in endothelial cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50% Ham's F12 w/o GHT: low glucose, and 50% DMEM without glycine: with NaHCO<sub>3</sub>, 1% glutamine, 10 mM HEPES, 10% FBS, 10 ng/ml bFGF) were plated on 96-well microtiter plates at a cell density of  $1 \times 10^4$  cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100  $\mu$ l/well test samples and controls (positive control = growth media; negative control = Protein 32 buffer = 10 mM HEPES, 140 mM NaCl, 4% (w/v) mannitol, pH 6.8). The cells were incubated for 30 minutes at 37°C, in 5% CO<sub>2</sub>. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed, where each capitalized reagent/buffer listed below was available from the kit.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100  $\mu$ l of Capture Hybridization Buffer was added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100  $\mu$ l of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortexed on the #2 setting for one minute. 80  $\mu$ l of the lysate was removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the plates were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/ $\mu$ l) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50  $\mu$ l of Amplifier Working Solution was added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/ $\mu$ l) in AL Hybridization Buffer. After the 10-minute cool-down period, the amplifier hybridization mixture was removed and the plates were washed twice with Wash A. 50  $\mu$ l of Label Probe Working Solution was added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room

temperature. Upon addition of 3  $\mu$ l of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three times with Wash D. 50  $\mu$ l of the Substrate Solution with Enhancer was added to each well. The plates were incubated for 30 minutes at 37°C and RLU was read in an appropriate luminometer.

5           The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the negative control (Protein 32/HEPES buffer described above) value was indicated by chemiluminescence units (RLU). The results are considered positive if the PRO polypeptide exhibits at least a two-fold value over the negative buffer control. Negative control = 1.00 RLU at 1.00% dilution. Positive control = 8.39 RLU at 1.00% dilution.

10           The following PRO polypeptides tested positive in this assay: PRO535, PRO826, PRO819, PRO1126, PRO1160 and PRO1387.

EXAMPLE 155: Inhibitory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 67)

15           This example shows that one or more of the polypeptides of the invention are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

          The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

20           More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

          The assay is prepared by plating in triplicate wells a mixture of:

          100:1 of test sample diluted to 1% or to 0.1%,

          50 :1 of irradiated stimulator cells, and

30           50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

35           In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000

rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to  $1 \times 10^7$  cells/ml of assay media. The assay is then conducted as described above.

Any decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein.

5           The following polypeptide tested positive in this assay: PRO1114, PRO836, PRO1159, PRO1312, PRO1192, PRO1195 and PRO1387.

EXAMPLE 156: Mouse Kidney Mesangial Cell Proliferation Assay (Assay 92)

10           This assay shows that certain polypeptides of the invention act to induce proliferation of mammalian kidney mesangial cells and, therefore, are useful for treating kidney disorders associated with decreased mesangial cell function such as Berger disease or other nephropathies associated with Schönlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohn disease. The assay is performed as follows. On day one, mouse kidney mesangial cells are plated on a 96 well plate in growth media (3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95% fetal bovine serum, 5% supplemented with 14 mM HEPES) and grown overnight. On day 2, PRO polypeptides are diluted at 2 concentrations (1% and 0.1%) in serum-free medium and added to the cells. Control samples are serum-free medium alone. On day 4, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Progenia) was added to each well and the colorimetric reaction was allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is anything that gives an absorbance reading which is at least 15% above the control reading.

20           The following polypeptide tested positive in this assay: PRO819, PRO813 and PRO1066.

EXAMPLE 157: Pericyte c-Fos Induction (Assay 93)

25           This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100  $\mu$ l of PRO polypeptide test samples and controls (positive control = DME+5% serum +/- PDGF at 500 ng/ml; negative control = protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading verses frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media = low glucose DMEM = 20% FBS + 1X pen strep + 1X fungizone. Assay Media = low glucose DMEM + 5% FBS.

35           The following polypeptides tested positive in this assay: PRO943 and PRO819.

EXAMPLE 158: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1114, PRO1007, PRO1066, PRO848, PRO1182, PRO1198, PRO1192, PRO1271, PRO1375 and PRO1387.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1184, PRO1360, PRO1309, PRO1154, PRO1181, PRO1186, PRO1160 and PRO1384.

EXAMPLE 159: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 µl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1282, PRO1310, PRO619, PRO943, PRO820, PRO1080, PRO1016, PRO1007, PRO1056, PRO791, PRO1111, PRO1184, PRO1360, PRO1309, PRO1107, PRO1132, PRO1131, PRO848, PRO1181, PRO1186, PRO1159, PRO1312, PRO1192 and PRO1384.

**EXAMPLE 160: Chondrocyte Proliferation Assay (Assay 111)**

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

5 Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm<sup>2</sup> every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 µl/well. After 5 days at 37°C, 20 µl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 µl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

15 The following PRO polypeptides tested positive in this assay: PRO1310, PRO844, PRO1312, PRO1192 and PRO1387.

**EXAMPLE 161: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)**

20 This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is a transcription factor called Pdx1.

25 The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20 µg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

35 14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 µg/ml

Aprotinin (50µg/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60µg/ml

5 Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100µg (BRL 100004)

Triiodothyronine, 10µl of  $5 \times 10^{-6}$  M (Sigma T5516)

10 Ethanolamine, 100µl of  $10^{-1}$  M (Sigma E0135)

Phosphoethanolamine, 100µl of  $10^{-1}$  M (Sigma P0503)

Selenium, 4µl of  $10^{-1}$  M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2µl of  $5 \times 10^{-3}$  M (Sigma #H0135)

15 Progesterone, 100µl of  $1 \times 10^{-3}$  M (Sigma #P6149)

Forskolin, 500µl of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10 µg/ml), insulin (1 µg/ml), gentamycin (100 ng/ml), aprotinin (50 µg/ml) and BPE (15 µg/ml).

20 Defined media:

RPMI 1640 plus transferrin (10 µg/ml), insulin (1 µg/ml), gentamycin (100 ng/ml) and aprotinin (50 µg/ml).

The following polypeptides tested positive in this assay: PRO1310, PRO1188, PRO1131 and PRO1387.

25

EXAMPLE 162: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

30 This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

35 In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay

if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO358, PRO1016, PRO1007, PRO826, PRO1066, PRO1029 and PRO1309.

EXAMPLE 163: Fetal Hemoglobin Induction in an Erythroblastic Cell Line (Assay 107)

5 This assay is useful for screening PRO polypeptides for the ability to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line. Molecules testing positive in this assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. The assay is performed as follows. Erythroblastic cells are plated in standard growth medium at 1000 cells/well in a 96 well format. PRO polypeptides are added to the growth medium at a  
10 concentration of 0.2% or 2% and the cells are incubated for 5 days at 37°C. As a positive control, cells are treated with 100µM hemin and as a negative control, the cells are untreated. After 5 days, cell lysates are prepared and analyzed for the expression of gamma globin (a fetal marker). A positive in the assay is a gamma globin level at least 2-fold above the negative control.

15 The following polypeptides tested positive in this assay: PRO1114, PRO826, PRO1066, PRO844, PRO1192 and PRO1358.

EXAMPLE 164: Induction of Pancreatic β-Cell Precursor Differentiation (Assay 89)

This assay shows that certain polypeptides of the invention act to induce differentiation of pancreatic β-cell precursor cells into mature pancreatic β-cells and, therefore, are useful for treating various insulin  
20 deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is insulin.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with  
25 collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20µg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed  
30 and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

- 35 group A 1:1000  
group B 1:1000  
recombinant human insulin 10 µg/ml

Aprotinin (50 $\mu$ g/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 $\mu$ g/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

5 Epidermal Growth Factor, 100 $\mu$ g (BRL 100004)

Triiodothyronine, 10 $\mu$ l of 5x10<sup>-6</sup> M (Sigma T5516)

Ethanolamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma E0135)

Phosphoethalamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma P0503)

Selenium, 4 $\mu$ l of 10<sup>-1</sup> M (Aesar #12574)

10 Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 $\mu$ l of 5X10<sup>-3</sup> M (Sigma #H0135)

Progesterone, 100 $\mu$ l of 1X10<sup>-3</sup> M (Sigma #P6149)

Forskolin, 500 $\mu$ l of 20mM (Calbiochem #344270)

Minimal media:

15 RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml), aprotinin (50  $\mu$ g/ml) and BPE (15  $\mu$ g/ml).

Defined media:

RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml) and aprotinin (50  $\mu$ g/ml).

20 The following polypeptides were positive in this assay: PRO1188, PRO1132, PRO1131 and PRO1181.

#### EXAMPLE 165: Skin Vascular Permeability Assay (Assay 64)

25 This assay shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Compounds which stimulate an immune response are useful therapeutically where stimulation of an immune response is beneficial. This skin vascular permeability assay is conducted as follows. Hairless guinea pigs weighing 350 grams or more are anesthetized with ketamine (75-80 mg/Kg) and 5 mg/Kg xylazine intramuscularly (IM). A sample of purified polypeptide of the invention or a conditioned media test sample

30 is injected intradermally onto the backs of the test animals with 100  $\mu$ l per injection site. It is possible to have about 10-30, preferably about 16-24, injection sites per animal. One  $\mu$ l of Evans blue dye (1 % in physiologic buffered saline) is injected intracardially. Blemishes at the injection sites are then measured (mm diameter) at 1 hr and 6 hr post injection. Animals were sacrificed at 6 hrs after injection. Each skin injection site is biopsied and fixed in formalin. The skins are then prepared for histopathologic evaluation. Each site is

35 evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least a minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is



scored as negative.

The following polypeptide tested positive in this assay: PRO1007, PRO1358 and PRO1375.

EXAMPLE 166: Induction of Endothelial Cell Apoptosis (ELISA) (Assay 109)

5 The ability of PRO polypeptides to induce apoptosis in endothelial cells was tested in human venous umbilical vein endothelial cells (HUVEC, Cell Systems) using a 96-well format, in 0% serum media supplemented with 100 ng/ml VEGF, 0.1% BSA, 1X penn/strep. A positive result in this assay indicates the usefulness of the polypeptide for therapeutically treating any of a variety of conditions associated with undesired endothelial cell growth including, for example, the inhibition of tumor growth. The 96-well plates used were manufactured by Falcon (No. 3072). Coating of 96 well plates were prepared by allowing  
10 gelatinization to occur for >30 minutes with 100  $\mu$ l of 0.2% gelatin in PBS solution. The gelatin mix was aspirated thoroughly before plating HUVEC cells at a final concentration of  $2 \times 10^4$  cells/ml in 10% serum containing medium - 100  $\mu$ l volume per well. The cells were grown for 24 hours before adding test samples containing the PRO polypeptide of interest.

15 To all wells, 100  $\mu$ l of 0% serum media (Cell Systems) complemented with 100 ng/ml VEGF, 0.1% BSA, 1X penn/strep was added. Test samples containing PRO polypeptides were added in triplicate at dilutions of 1%, 0.33% and 0.11%. Wells without cells were used as a blank and wells with cells only were used as a negative control. As a positive control, 1:3 serial dilutions of 50  $\mu$ l of a 3x stock of staurosporine were used. The cells were incubated for 24 to 35 hours prior to ELISA.

20 ELISA was used to determine levels of apoptosis preparing solutions according to the Boehringer Manual [Boehringer, Cell Death Detection ELISA plus, Cat No. 1 920 685]. Sample preparations: 96 well plates were spun down at 1 krpm for 10 minutes (200g); the supernatant was removed by fast inversion, placing the plate upside down on a paper towel to remove residual liquid. To each well, 200  $\mu$ l of 1X Lysis buffer was added and incubation allowed at room temperature for 30 minutes without shaking. The plates were spun down for 10 minutes at 1 krpm, and 20  $\mu$ l of the lysate (cytoplasmic fraction) was transferred into  
25 streptavidin coated MTP. 80  $\mu$ l of immunoreagent mix was added to the 20  $\mu$ l lysate in each well. The MTP was covered with adhesive foil and incubated at room temperature for 2 hours by placing it on an orbital shaker (200 rpm). After two hours, the supernatant was removed by suction and the wells rinsed three times with 250  $\mu$ l of 1X incubation buffer per well (removed by suction). Substrate solution was added (100  $\mu$ l) into each well and incubated on an orbital shaker at room temperature at 250 rpm until color development was  
30 sufficient for a photometric analysis (approx. after 10-20 minutes). A 96 well reader was used to read the plates at 405 nm, reference wavelength, 492 nm. The levels obtained for PIN 32 (control buffer) was set to 100%. Samples with levels > 130% were considered positive for induction of apoptosis.

The following PRO polypeptides tested positive in this assay: PRO844.

35 EXAMPLE 167: Guinea Pig Vascular Leak (Assay 32)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce vascular permeability. Polypeptides testing positive in this assay are expected to be useful

for the therapeutic treatment of conditions which would benefit from enhanced vascular permeability including, for example, conditions which may benefit from enhanced local immune system cell infiltration.

Hairless guinea pigs weighing 350 grams or more were anesthetized with Ketamine (75-80 mg/kg) and 5 mg/kg Xylazine intramuscularly. Test samples containing the PRO polypeptide or a physiological buffer without the test polypeptide are injected into skin on the back of the test animals with 100  $\mu$ l per injection site intradermally. There were approximately 16-24 injection sites per animal. One ml of Evans blue dye (1% in PBS) is then injected intracardially. Skin vascular permeability responses to the compounds (*i.e.*, blemishes at the injection sites of injection) are visually scored by measuring the diameter (in mm) of blue-colored leaks from the site of injection at 1, 6 and 24 hours post administration of the test materials. The mm diameter of blueness at the site of injection is observed and recorded as well as the severity of the vascular leakage. Blemishes of at least 5 mm in diameter are considered positive for the assay when testing purified proteins, being indicative of the ability to induce vascular leakage or permeability. A response greater than 7 mm diameter is considered positive for conditioned media samples. Human VEGF at 0.1  $\mu$ g/100  $\mu$ l is used as a positive control, inducing a response of 4-8 mm diameter.

The following PRO polypeptides tested positive in this assay: PRO1155.

EXAMPLE 168: Mouse Mesengial Cell Inhibition Assay (Assay 114)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to inhibit the proliferation of mouse mesengial cells in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of such diseases or conditions where inhibition of mesengial cell proliferation would be beneficial such as, for example, cystic renal dysplasia, polycystic kidney disease, or other kidney disease associated with abnormal mesengial cell proliferation, renal tumors, and the like.

On day 1, mouse mesengial cells are plated on a 96 well plate in growth medium (a 3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95%; fetal bovine serum, 5%; supplemented with 14mM HEPES) and then are allowed to grow overnight. On day 2, the PRO polypeptide is diluted at 2 different concentrations (1%, 0.1%) in serum-free medium and is added to the cells. The negative control is growth medium without added PRO polypeptide. After the cells are allowed to incubate for 48 hours, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Promega) is added to each well and the colormetric reaction is allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is an absorbance reading which is at least 10% above the negative control.

The following PRO polypeptides tested positive in this assay: PRO1192 and PRO1195.

Example 169: In Vitro Antitumor Assay (Assay 161)

The antiproliferative activity of various PRO polypeptides was determined in the investigational, disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., *J. Natl. Cancer Inst.* 82:1107-1112 (1990). The 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions

for their maintenance and culture *in vitro* have been described by Monks et al., *J. Natl. Cancer Inst.* 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, *Cancer: Princ. Pract. Oncol. Update* 3(10):1-12 [1989]).

Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco), washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100  $\mu$ L volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero in 100  $\mu$ L aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log dilutions (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO<sub>2</sub> atmosphere and 100% humidity.

After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid to remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris base [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The results are shown in the following table, where the abbreviations are as follows:

NSCL = non-small cell lung carcinoma

CNS = central nervous system

Table 7

|    | Test compound | Concentration | Days | Tumor Cell Line Type | Cell Line   |
|----|---------------|---------------|------|----------------------|-------------|
|    |               |               |      |                      | Designation |
| 25 | PRO1016       | 0.1 nM        | 2    | Leukemia             | K-568       |
|    | PRO1016       | 0.1 nM        | 2    | Leukemia             | MOLT-4      |
|    | PRO1016       | 0.1 nM        | 2    | Leukemia             | RPMI-8226   |
|    | PRO1016       | 0.1 nM        | 2    | NSCL                 | A549/ATCC   |
| 30 | PRO1016       | 0.1 nM        | 2    | NSCL                 | EKVX        |
|    | PRO1016       | 0.1 nM        | 2    | NSCL                 | NCI-H23     |
|    | PRO1016       | 0.1 nM        | 2    | NSCL                 | NCI-H522    |
|    | PRO1016       | 0.1 nM        | 2    | Colon                | KM-12       |
| 35 | PRO1016       | 0.1 nM        | 2    | CNS                  | SF-295      |
|    | PRO1016       | 0.1 nM        | 2    | Melanoma             | SK-MEL-5    |
|    | PRO1016       | 0.1 nM        | 2    | Melanoma             | UACC-257    |
|    | PRO1016       | 0.1 nM        | 2    | Ovarian              | OVCAR-3     |
| 40 | PRO1016       | 0.1 nM        | 2    | Ovarian              | OVCAR-4     |
|    | PRO1016       | 0.1 nM        | 2    | Breast               | NCI/SDR-RES |
|    | PRO1016       | 0.1 nM        | 2    | Breast               | T-47D       |
|    | PRO1016       | 0.1 nM        | 6    | Leukemia             | CCRF-CEM    |
|    | PRO1016       | 0.1 nM        | 6    | Leukemia             | K-562       |

Table 7 (cont')

|    | Test compound | Concentration | Days | Tumor Cell Line Type | Cell Line           |
|----|---------------|---------------|------|----------------------|---------------------|
|    |               |               |      |                      | Designation         |
| 5  | PRO1016       | 0.1 nM        | 6    | Leukemia             | MOLT-4              |
|    | PRO1016       | 0.1 nM        | 6    | Leukemia             | RPMI-8226           |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | A549/ATCC           |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | EKVX                |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | HOP-62              |
| 10 | PRO1016       | 0.1 nM        | 6    | NSCL                 | NCI-H23             |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | NCI-H322M           |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | NCI-H460            |
|    | PRO1016       | 0.1 nM        | 6    | NSCL                 | NCI-H522            |
|    | PRO1016       | 0.1 nM        | 6    | Colon                | COLO 205            |
| 15 | PRO1016       | 0.1 nM        | 6    | Colon                | CHT-116             |
|    | PRO1016       | 0.1 nM        | 6    | Colon                | HCT-15              |
|    | PRO1016       | 0.1 nM        | 6    | Colon                | HT-29               |
|    | PRO1016       | 0.1 nM        | 6    | Colon                | SW-620              |
|    | PRO1016       | 0.1 nM        | 6    | CNS                  | SF-295              |
| 20 | PRO1016       | 0.1 nM        | 6    | CNS                  | SF-539              |
|    | PRO1016       | 0.1 nM        | 6    | CNS                  | SNB-19              |
|    | PRO1016       | 0.1 nM        | 6    | CNS                  | U251                |
|    | PRO1016       | 0.1 nM        | 6    | Melanoma             | LOX IMVI            |
|    | PRO1016       | 0.1 nM        | 6    | Melanoma             | MALME-3M            |
| 25 | PRO1016       | 0.1 nM        | 6    | Melanoma             | SK-MEL-28           |
|    | PRO1016       | 0.1 nM        | 6    | Melanoma             | SK-MEL-5            |
|    | PRO1016       | 0.1 nM        | 6    | Melanoma             | UACC-257            |
|    | PRO1016       | 0.1 nM        | 6    | Melanoma             | UACC-62             |
|    | PRO1016       | 0.1 nM        | 6    | Ovarian              | IGROV1              |
| 30 | PRO1016       | 0.1 nM        | 6    | Ovarian              | OVCAR-3             |
|    | PRO1016       | 0.1 nM        | 6    | Ovarian              | OVCAR-4             |
|    | PRO1016       | 0.1 nM        | 6    | Ovarian              | OVCAR-8             |
|    | PRO1016       | 0.1 nM        | 6    | Renal                | ACHN                |
|    | PRO1016       | 0.1 nM        | 6    | Renal                | RXF 393             |
| 35 | PRO1016       | 0.1 nM        | 6    | Renal                | SN12C               |
|    | PRO1016       | 0.1 nM        | 6    | Renal                | TK-10               |
|    | PRO1016       | 0.1 nM        | 6    | Prostate             | PC-3                |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | MCF-7               |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | NCI/ADR-RES         |
| 40 | PRO1016       | 0.1 nM        | 6    | Breast               | MDA-MB-231          |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | MDA-MB-435          |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | MDA-N               |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | BT-549              |
|    | PRO1016       | 0.1 nM        | 6    | Breast               | T-47D               |
| 45 | PRO1186       | 95 nM         | 2    | NSCL                 | NCI-H226            |
|    | PRO1186       | 95 nM         | 2    | Colon                | Colo205             |
|    | PRO1186       | 2.2 nM        | 6    | Breast               | MDA-N               |
|    | PRO1186       | 114 nM        | 2    | NSCL                 | NCI-H322M           |
|    | PRO1186       | 114 nM        | 2    | CNS                  | SF-268; SF-539      |
| 50 | PRO1186       | 114 nM        | 2    | Ovarian              | IGFOV1              |
|    | PRO1186       | 114 nM        | 2    | Renal                | 786-0; SN12C; TK-10 |
|    | PRO1186       | 114 nM        | 6    | Leukemia             | MOLT-4; RPMI-8226   |
|    | PRO1186       | 114 nM        | 6    | Melanoma             | LOX IMVI            |
|    | PRO1186       | 114 nM        | 6    | Ovarian              | OVCAR-4; SK-OV-3    |

Table 7 (cont')

|    | Test compound | Concentration | Days | Tumor Cell Line Type | C e l l L i n e   |
|----|---------------|---------------|------|----------------------|-------------------|
|    |               |               |      |                      | Designation       |
|    | PRO1186       | 114 nM        | 6    | Breast               | MDA-MB-435; T-47D |
| 5  | PRO1186       | 8.1 nM        | 6    | Leukemia             | K-562             |
|    | PRO1186       | 8.1 nM        | 6    | NSCL                 | HOP-62            |
|    | PRO1186       | 8.1 nM        | 6    | Colon                | Colo205; HCC-2998 |
|    | PRO1186       | 8.1 nM        | 6    | Breast               | T-47D             |
|    | PRO1186       | 15.4 nM       | 6    | Leukemia             | K-562             |
| 10 | PRO1186       | 3.6 nM        | 2    | Ovarian              | OVCAR-3           |
|    | PRO1186       | 3.6 nM        | 6    | NSCL                 | HOP-62            |

The results of these assays demonstrate that the positive testing PRO polypeptides are useful for inhibiting neoplastic growth in a number of different tumor cell types and may be used therapeutically therefor.. Antibodies against these PRO polypeptides are useful for affinity purification of these useful polypeptides. Nucleic acids encoding these PRO polypeptides are useful for the recombinant preparation of these polypeptides.

#### EXAMPLE 170: Gene Amplification in Tumors

This example shows that certain PRO polypeptide-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers and diagnostic determination of the presence of those cancers. Therapeutic agents may take the form of antagonists of the PRO polypeptide, for example, murine-human chimeric, humanized or human antibodies against a PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 8 and the primary tumors and cell lines referred to throughout this example are given below.

The results of the TaqMan™ are reported in delta ( $\Delta$ ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TaqMan™ fluorescent probe derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide-encoding gene which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are

preferred for the primer and probe derivation, e.g., 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO polypeptide gene amplification analysis were as follows:

PRO290 (DNA35680-1212):

35680.tm.p:

5 5'-CCACCAATGGCAGCCCCACCT-3' (SEQ ID NO:428)

35680.tm.f:

5'-GACTGCCCTCCCTGCCA-3' (SEQ ID NO:429)

35680.tm.r:

10 5'-CAAAAAGCCTGGAAGTCTTCAAAG-3' (SEQ ID NO:430)

PRO341 (DNA26288-1239):

26288.tm.fl:

5'-CAGCTGGACTGCAGGTGCTA-3' (SEQ ID NO:431)

26288.tm.rl:

15 5'-CAGTGAGCACAGCAAGTGTCCCT-3' (SEQ ID NO:432)

26288.tm.pl:

5'-GGCCACCTCCTTGAGTCTTCAGTTCCT-3' (SEQ ID NO:433)

PRO535 (DNA49143-1429):

20 49143.tm.fl:

5'-CAACTACTGGCTAAAGCTGGTGAA-3' (SEQ ID NO:434)

49143.tm.rl:

5'-CCTTTCTGTATAGGTGATACCCAATGA-3' (SEQ ID NO:435)

49143.tm.pl:

25 5'-TGGCCATCCCTACCAGAGGCAAAA-3' (SEQ ID NO:436)

PRO619 (DNA49821-1562):

49821.tm.fl:

5'-CTGAAGACGACGCGGATTACTA-3' (SEQ ID NO:437)

30 49821.tm.rl:

5'-GGCAGAAATGGGAGGCAGA-3' (SEQ ID NO:438)

49821.tm.pl:

5'-TGCTCTGTTGGCTACGGCTTTAGTCCCTAG-3' (SEQ ID NO:439)

35 PRO809 (DNA57836-1338):

57836.tm.fl:

5'-AGCAGCAGCCATGTAGAATGAA-3' (SEQ ID NO:440)

- 57836.tm.rl:  
5'-AATACGAACAGTGCACGCTGAT-3' (SEQ ID NO:441)  
57836.tm.pl:  
5'-TCCAGAGAGCCAAGCACGGCAGA-3' (SEQ ID NO:442)
- 5 PRO830 (DNA56866-1342):  
56866.tm.fl:  
5'-TCTAGCCAGCTTGGCTCCAATA-3' (SEQ ID NO:443)  
56866.tm.rl:  
5'-CCTGGCTCTAGCACCAACTCATA-3' (SEQ ID NO:444)  
10 56866.tm.pl:  
5'-TCAGTGGCCCTAAGGAGATGGGCCT-3' (SEQ ID NO:445)
- PRO848 (DNA59839-1461):  
59839.tm.fl:  
15 5'-CAGGATACAGTGGGAATCTTGAGA-3' (SEQ ID NO:446)  
59839.tm.rl:  
5'-CCTGAAGGGCTTGGAGCTTAGT-3' (SEQ ID NO:447)  
59839.tm.pl:  
5'-TCTTTGGCCATTTCCCATGGCTCA-3' (SEQ ID NO:448)  
20
- PRO943 (DNA52192-1369):  
52192.tm.fl:  
5'-CCCATGGCGAGGAGGAAT-3' (SEQ ID NO:449)  
52192.tm.rl:  
25 5'-TGC GTACGTGTGCCTTCAG-3' (SEQ ID NO:450)  
52192.tm.pl:  
5'-CAGCACCCAGGCAGTCTGTGTGT-3' (SEQ ID NO:451)
- PRO1005 (DNA57708-1411):  
30 57708.tm.fl:  
5'-AACGTGCTACACGACCAGTGTACT-3' (SEQ ID NO:452)  
57708.tm.rl:  
5'-CACAGCATATTCAGATGACTAAATCCA-3' (SEQ ID NO:453)  
57708.tm.pl:  
35 5'-TTGTTTAGTTCTCCACCGTGTCTCCACAGAA-3' (SEQ ID NO:454)

PRO1009 (DNA57129-1413):57129.tm.fl:

5'-TGTCAGAATGCAACCTGGCTT-3' (SEQ ID NO:455)

57129.tm.rl:

5'-TGATGTGCCTGGCTCAGAAC-3' (SEQ ID NO:456)

5 57129.tm.pl:

5'-TGCACCTAGATGTCCCCAGCACCC-3' (SEQ ID NO:457)

PRO1097 (DNA59841-1460):59841.tm.fl:

10 5'-AAGATGCGCCAGGCTTCTTA-3' (SEQ ID NO:458)

59841.tm.rl:

5'-CTCCTGTACGGTCTGCTCACTTAT-3' (SEQ ID NO:459)

59841.tm.pl:

15 5'-TGGCTGTCAGTCCAGTGTGCATGG-3' (SEQ ID NO:460)

PRO1107 (DNA59606-1471):59606.tm.fl:

5'-GCATAGGGATAGATAAGATCCTGCTTTAT-3' (SEQ ID NO:461)

59606.tm.rl:

20 5'-CAAATTAAAGTACCCATCAGGAGAGAA-3' (SEQ ID NO:462)

59606.tm.pl:

5'-AAGTTGCTAAATATATACATTATCTGCGCCAAGTCCA-3' (SEQ ID NO:463)

PRO1111 (DNA58721-1475):25 58721.tm.fl:

5'-GTGCTGCCCACAATTCATGA-3' (SEQ ID NO:464)

58721.tm.rl:

5'-GTCCTTGGTATGGGTCTGAATTATAT-3' (SEQ ID NO:465)

58721.tm.pl:

30 5'-ACTCTCTGCACCCACAGTCACCACTATCTC-3' (SEQ ID NO:466)

PRO1153 (DNA59842-1502):59842.tm.fl:

5'-CTGAGGAACCAGCCATGTCTCT-3' (SEQ ID NO:467)

35 59842.tm.rl:

5'-GACCAGATGCAGGTACAGGATGA-3' (SEQ ID NO:468)



59842.tm.pl:

5'-CTGCCCCTTCAGTGATGCCAACCTT-3' (SEQ ID NO:469)

PRO1182 (DNA59848-1512):59848.tm.fl:

5 5'-GGGTGGAGGCTCACTGAGTAGA-3' (SEQ ID NO:470)

59848.tm.rl:

5'-CAATACAGGTAATGAACTCTGCTTCTT-3' (SEQ ID NO:471)

59848.tm.pl:

10 5'-TCCTCTTAAGCATAGGCCATTTTCTCAGTTTAGACA-3' (SEQ ID NO:472)

PRO1184 (DNA59220-1514):59220.tm.fl:

5'-GGTGGTCTTGCTTGGTCTCAC-3' (SEQ ID NO:473)

59220.tm.rl:

15 5'-CCGTCGTTTCAGCAACATGAC-3' (SEQ ID NO:474)

59220.tm.pl:

5'-ACCGCCTACCGCTGTGCCCA-3' (SEQ ID NO:475)

PRO1187 (DNA62876-1517):

20 62876.tm.fl:

5'-CAGTAAACCACAGGCTGGATTT-3' (SEQ ID NO:476)

62876.tm.rl:

5'-CCTGAGAGCAAGAAGGTTGAGAAT-3' (SEQ ID NO:477)

62876.tm.pl:

25 5'-TAGACAGGGACCATGGCCCGCA-3' (SEQ ID NO:478)

PRO1281 (DNA59820-1549):59820.tm.fl:

5'-TGGGCTGTAGAAGAGTTGTTG-3' (SEQ ID NO:479)

30 59820.tm.rl:

5'-TCCACACTTGGCCAGTTTAT-3' (SEQ ID NO:480)

59820.tm.pl:

5'-CCCAACTTCTCCCTTTTGGACCCT-3' (SEQ ID NO:481)

35 PRO1112 (DNA57702-1476):

57702.tm.fl

5'-GTCCCITCACTGTTTAGAGCATGA-3' (SEQ ID NO:482)

57702.tm.pl

5'-ACTCTCCCCCTCAACAGCCTCCTGAG-3' (SEQ ID NO:483)

57702.tm.r1

5'-GTGGTCAGGGCAGATCCTTT-3' (SEQ ID NO:484)

5 PRO1185 (DNA62881-1515):62881.tm.f1:

5'-ACAGATCCAGGAGAGACTCCACA -3' (SEQ ID NO:485)

62881.tm.pl:

5'-AGCGGCGCTCCCAGCCTGAAT -3' (SEQ ID NO:486)

10 62881.tm.r1:

5'-CATGATTGGTCCTCAGTTCCATC -3' (SEQ ID NO:487)

PRO1245 (DNA64884-1527):64884.tm.f1:

15 5'-ATAGAGGGCTCCCAGAAGTG -3' (SEQ ID NO:488)

64884.tm.pl:

5'-CAGGGCCTTCAGGGCCTTCAC-3' (SEQ ID NO:489)

64884.tm.r1:

5'-GCTCAGCCAAACACTGTCA-3' (SEQ ID NO:490)

20 64884.tm.f2:

5'-GGGGCCCTGACAGTGTT -3' (SEQ ID NO:491)

64884.tm.p2:

5'-CTGAGCCGAGACTGGAGCATCTACAC-3' (SEQ ID NO:492)

64884.tm.r2:

25 5'-GTGGGCAGCGTCTTGTC-3' (SEQ ID NO:493)

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers (forward [.f] and reverse [.r]) are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe (.p), is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700TM Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The  $\Delta C_t$  values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results.

Table 8 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO polypeptide compounds of the invention.

Table 8  
Primary Lung and Colon Tumor Profiles

|    | Primary Tumor Stage                          | Stage | Other Stage | Dukes Stage | T Stage | N Stage |
|----|--|-------|-------------|-------------|---------|---------|
| 5  | Human lung tumor AdenoCa (SRCC724) [LT1]     | IIA   |             |             | T1      | N1      |
|    | Human lung tumor SqCCa (SRCC725) [LT1a]      | IIB   |             |             | T3      | N0      |
|    | Human lung tumor AdenoCa (SRCC726) [LT2]     | IB    |             |             | T2      | N0      |
|    | Human lung tumor AdenoCa (SRCC727) [LT3]     | IIIA  |             |             | T1      | N2      |
|    | Human lung tumor AdenoCa (SRCC728) [LT4]     | IB    |             |             | T2      | N0      |
| 10 | Human lung tumor SqCCa (SRCC729) [LT6]       | IB    |             |             | T2      | N0      |
|    | Human lung tumor Aden/SqCCa (SRCC730) [LT7]  | IA    |             |             | T1      | N0      |
|    | Human lung tumor AdenoCa (SRCC731) [LT9]     | IB    |             |             | T2      | N0      |
|    | Human lung tumor SqCCa (SRCC732) [LT10]      | IIB   |             |             | T2      | N1      |
|    | Human lung tumor SqCCa (SRCC733) [LT11]      | IIA   |             |             | T1      | N1      |
| 15 | Human lung tumor AdenoCa (SRCC734) [LT12]    | IV    |             |             | T2      | N0      |
|    | Human lung tumor AdenoSqCCa (SRCC735) [LT13] | IIB   |             |             | T2      | N0      |
|    | Human lung tumor SqCCa (SRCC736) [LT15]      | IB    |             |             | T2      | N0      |
|    | Human lung tumor SqCCa (SRCC737) [LT16]      | IB    |             |             | T2      | N0      |
|    | Human lung tumor SqCCa (SRCC738) [LT17]      | IIB   |             |             | T2      | N1      |
| 20 | Human lung tumor SqCCa (SRCC739) [LT18]      | IB    |             |             | T2      | N0      |
|    | Human lung tumor SqCCa (SRCC740) [LT19]      | IB    |             |             | T2      | N0      |
|    | Human lung tumor LCCa (SRCC741) [LT21]       | IIB   |             |             | T3      | N1      |
|    | Human lung AdenoCa (SRCC811) [LT22]          | IA    |             |             | T1      | N0      |
|    | Human colon AdenoCa (SRCC742) [CT2]          |       | M1          | D           | pT4     | N0      |
| 25 | Human colon AdenoCa (SRCC743) [CT3]          |       |             | B           | pT3     | N0      |
|    | Human colon AdenoCa (SRCC744) [CT8]          |       |             | B           | T3      | N0      |
|    | Human colon AdenoCa (SRCC745) [CT10]         |       |             | A           | pT2     | N0      |
|    | Human colon AdenoCa (SRCC746) [CT12]         |       | MO, R1      | B           | T3      | N0      |
|    | Human colon AdenoCa (SRCC747) [CT14]         |       | pMO, RO     | B           | pT3     | pN0     |
| 30 | Human colon AdenoCa (SRCC748) [CT15]         |       | M1, R2      | D           | T4      | N2      |
|    | Human colon AdenoCa (SRCC749) [CT16]         |       | pMO         | B           | pT3     | pN0     |
|    | Human colon AdenoCa (SRCC750) [CT17]         |       |             | C1          | pT3     | pN1     |
|    | Human colon AdenoCa (SRCC751) [CT1]          |       | MO, R1      | B           | pT3     | N0      |
|    | Human colon AdenoCa (SRCC752) [CT4]          |       |             | B           | pT3     | M0      |
| 35 | Human colon AdenoCa (SRCC753) [CT5]          |       | G2          | C1          | pT3     | pN0     |
|    | Human colon AdenoCa (SRCC754) [CT6]          |       | pMO, RO     | B           | pT3     | pN0     |
|    | Human colon AdenoCa (SRCC755) [CT7]          |       | G1          | A           | pT2     | pN0     |
|    | Human colon AdenoCa (SRCC756) [CT9]          |       | G3          | D           | pT4     | pN2     |
|    | Human colon AdenoCa (SRCC757) [CT11]         |       |             | B           | T3      | N0      |
| 40 | Human colon AdenoCa (SRCC758) [CT18]         |       | MO, RO      | B           | pT3     | pN0     |

#### DNA Preparation:

DNA was prepared from cultured cell lines, primary tumors, normal human blood. The isolation was performed using purification kit, buffer set and protease and all from Quiagen, according to the manufacturer's instructions and the description below.

#### 45 Cell culture lysis:

Cells were washed and trypsinized at a concentration of  $7.5 \times 10^8$  per tip and pelleted by centrifuging at 1000 rpm for 5 minutes at 4°C, followed by washing again with 1/2 volume of PBS recentrifugation. The pellets were washed a third time, the suspended cells collected and washed 2x with PBS. The cells were then suspended into 10 ml PBS. Buffer C1 was equilibrated at 4°C. Qiagen protease #19155 was diluted into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and equilibrated at 4°C. 10 ml of G2 Buffer was prepared

by diluting Qiagen RNase A stock (100 mg/ml) to a final concentration of 200  $\mu$ g/ml.

Buffer C1 (10 ml, 4°C) and ddH<sub>2</sub>O (40 ml, 4°C) were then added to the 10 ml of cell suspension, mixed by inverting and incubated on ice for 10 minutes. The cell nuclei were pelleted by centrifuging in a Beckman swinging bucket rotor at 2500 rpm at 4°C for 15 minutes. The supernatant was discarded and the nuclei were suspended with a vortex into 2 ml Buffer C1 (at 4°C) and 6 ml ddH<sub>2</sub>O, followed by a second 4°C centrifugation at 2500 rpm for 15 minutes. The nuclei were then resuspended into the residual buffer using 200  $\mu$ l per tip. G2 buffer (10 ml) was added to the suspended nuclei while gentle vortexing was applied. Upon completion of buffer addition, vigorous vortexing was applied for 30 seconds. Quiagen protease (200  $\mu$ l, prepared as indicated above) was added and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Solid human tumor sample preparation and lysis:*

Tumor samples were weighed and placed into 50 ml conical tubes and held on ice. Processing was limited to no more than 250 mg tissue per preparation (1 tip/preparation). The protease solution was freshly prepared by diluting into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer (20 ml) was prepared by diluting DNase A to a final concentration of 200 mg/ml (from 100 mg/ml stock). The tumor tissue was homogenated in 19 ml G2 buffer for 60 seconds using the large tip of the polytron in a laminar-flow TC hood in order to avoid inhalation of aerosols, and held at room temperature. Between samples, the polytron was cleaned by spinning at 2 x 30 seconds each in 2L ddH<sub>2</sub>O, followed by G2 buffer (50 ml). If tissue was still present on the generator tip, the apparatus was disassembled and cleaned.

Quiagen protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation was repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Human blood preparation and lysis:*

Blood was drawn from healthy volunteers using standard infectious agent protocols and citrated into 10 ml samples per tip. Quiagen protease was freshly prepared by dilution into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer was prepared by diluting RNase A to a final concentration of 200  $\mu$ g/ml from 100 mg/ml stock. The blood (10 ml) was placed into a 50 ml conical tube and 10 ml C1 buffer and 30 ml ddH<sub>2</sub>O (both previously equilibrated to 4°C) were added, and the components mixed by inverting and held on ice for 10 minutes. The nuclei were pelleted with a Beckman swinging bucket rotor at 2500 rpm, 4°C for 15 minutes and the supernatant discarded. With a vortex, the nuclei were suspended into 2 ml C1 buffer (4°C) and 6 ml ddH<sub>2</sub>O (4°C). Vortexing was repeated until the pellet was white. The nuclei were then suspended into the residual buffer using a 200  $\mu$ l tip. G2 buffer (10 ml) were added to the suspended nuclei while gently vortexing, followed by vigorous vortexing for 30 seconds. Quiagen protease was added (200  $\mu$ l) and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Purification of cleared lysates:*(1) Isolation of genomic DNA:

Genomic DNA was equilibrated (1 sample per maxi tip preparation) with 10 ml QBT buffer. QF elution buffer was equilibrated at 50°C. The samples were vortexed for 30 seconds, then loaded onto equilibrated tips and drained by gravity. The tips were washed with 2 x 15 ml QC buffer. The DNA was  
5 eluted into 30 ml silanized, autoclaved 30 ml Corex tubes with 15 ml QF buffer (50°C). Isopropanol (10.5 ml) was added to each sample, the tubes covered with parafin and mixed by repeated inversion until the DNA precipitated. Samples were pelleted by centrifugation in the SS-34 rotor at 15,000 rpm for 10 minutes at 4°C. The pellet location was marked, the supernatant discarded, and 10 ml 70% ethanol (4°C) was added. Samples were pelleted again by centrifugation on the SS-34 rotor at 10,000 rpm for 10 minutes at 4°C. The pellet  
10 location was marked and the supernatant discarded. The tubes were then placed on their side in a drying rack and dried 10 minutes at 37°C, taking care not to overdry the samples.

After drying, the pellets were dissolved into 1.0 ml TE (pH 8.5) and placed at 50°C for 1-2 hours. Samples were held overnight at 4°C as dissolution continued. The DNA solution was then transferred to 1.5 ml tubes with a 26 gauge needle on a tuberculin syringe. The transfer was repeated 5x in order to shear the  
15 DNA. Samples were then placed at 50°C for 1-2 hours.

(2) Quantitation of genomic DNA and preparation for gene amplification assay:

The DNA levels in each tube were quantified by standard  $A_{260}$ ,  $A_{280}$  spectrophotometry on a 1:20 dilution (5  $\mu$ l DNA + 95  $\mu$ l ddH<sub>2</sub>O) using the 0.1 ml quartz cuvetts in the Beckman DU640 spectrophotometer.  $A_{260}/A_{280}$  ratios were in the range of 1.8-1.9. Each DNA samples was then diluted further  
20 to approximately 200 ng/ml in TE (pH 8.5). If the original material was highly concentrated (about 700 ng/ $\mu$ l), the material was placed at 50°C for several hours until resuspended.

Fluorometric DNA quantitation was then performed on the diluted material (20-600 ng/ml) using the manufacturer's guidelines as modified below. This was accomplished by allowing a Hoeffer DyNA Quant 200 fluorometer to warm-up for about 15 minutes. The Hoechst dye working solution (#H33258, 10  $\mu$ l, prepared  
25 within 12 hours of use) was diluted into 100 ml 1 x TNE buffer. A 2 ml cuvette was filled with the fluorometer solution, placed into the machine, and the machine was zeroed. pGEM 3Zf(+) (2  $\mu$ l, lot #360851026) was added to 2 ml of fluorometer solution and calibrated at 200 units. An additional 2  $\mu$ l of pGEM 3Zf(+) DNA was then tested and the reading confirmed at 400 +/- 10 units. Each sample was then read at least in triplicate. When 3 samples were found to be within 10% of each other, their average was taken  
30 and this value was used as the quantification value.

The fluorometrically determined concentration was then used to dilute each sample to 10 ng/ $\mu$ l in ddH<sub>2</sub>O. This was done simultaneously on all template samples for a single TaqMan plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with Taqman™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The  
35 diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough

for 8-9 plates or 64 tests.

*Gene amplification assay:*

The PRO polypeptide compounds of the invention were screened in the following primary tumors and the resulting  $\Delta C_t$  values greater than or equal to 1.0 are reported in Tables 9A-C below.

Table 9A

ΔCt values in lung and colon primary tumors and cell line models

| Primary Tumor | PRO290 | PRO341 | PRO535 | PRO619 | PRO1112 | PRO809 | PRO830 | PRO848 |
|---------------|--------|--------|--------|--------|---------|--------|--------|--------|
| LT-1a         | ---    | ---    | ---    | ---    | ---     | ---    | 1.13   | ---    |
| LT3           | ---    | ---    | ---    | 1.04   | ---     | ---    | ---    | ---    |
| LT7           | ---    | ---    | ---    | 1.68   | ---     | ---    | ---    | ---    |
| LT9           | ---    | ---    | ---    | 1.21   | ---     | ---    | ---    | ---    |
| LT10          | ---    | ---    | ---    | 1.34   | ---     | ---    | ---    | ---    |
| LT11          | 1.63   | ---    | 1.40   | 1.19   | ---     | ---    | ---    | ---    |
| LT12          | ---    | ---    | ---    | 1.34   | 1.135   | ---    | ---    | ---    |
| LT13          | 1.47   | ---    | 1.37   | 1.41   | 1.525   | 1.40   | 1.25   | 1.04   |
| LT15          | 1.67   | ---    | ---    | 2.02   | 1.195   | ---    | ---    | ---    |
| LT16          | ---    | 1.12   | ---    | 1.69   | 1.635   | 1.61   | 1.35   | 1.22   |
| LT17          | 1.22   | 1.33   | 1.42   | 1.57   | 1.74    | 1.03   | ---    | ---    |
| LT18          | ---    | ---    | ---    | 2.08   | 1.775   | ---    | ---    | ---    |
| LT19          | 2.07   | ---    | ---    | 1.52   | ---     | ---    | ---    | ---    |
| LT21          | ---    | 1.15   | ---    | ---    | 1.455   | 1.10   | 1.17   | ---    |
| CT2           | 1.56   | ---    | ---    | 1.83   | 1.255   | ---    | ---    | ---    |
|               |        |        |        | 1.67   | ---     | ---    | ---    | ---    |
|               |        |        |        | 1.32   | ---     | ---    | ---    | ---    |
|               |        |        |        | 1.14   | ---     | ---    | 1.31   | ---    |
|               |        |        |        | 2.33   | ---     | ---    | ---    | ---    |
|               |        |        |        | 1.90   | ---     | ---    | ---    | ---    |
|               |        |        |        | 1.15   | ---     | 1.05   | ---    | 1.07   |
|               |        |        |        | 1.09   | ---     | ---    | ---    | ---    |
|               |        |        |        | 1.22   | 2.265   | ---    | ---    | ---    |



Table 9A (cont')

ΔCt values in lung and colon primary tumors and cell line models

| Primary Tumor | PRO290 | PRO341 | PRO535 | PRO619 | PRO1112 | PRO809 | PRO830 | PRO848 |
|---------------|--------|--------|--------|--------|---------|--------|--------|--------|
| CT3           | ---    | ---    | 1.28   | 1.49   | ---     | ---    | ---    | ---    |
| CT8           | ---    | ---    | ---    | ---    | 1.065   | ---    | ---    | ---    |
| CT10          | ---    | ---    | 1.34   | ---    | 1.575   | ---    | ---    | ---    |
| CT12          | ---    | ---    | ---    | ---    | 1.315   | ---    | ---    | ---    |
| CT14          | ---    | ---    | 1.29   | ---    | 1.895   | ---    | ---    | ---    |
| CT15          | ---    | ---    | 1.10   | 1.00   | 1.465   | ---    | ---    | ---    |
| CT16          | ---    | ---    | 1.35   | 1.02   | 1.255   | ---    | ---    | ---    |
| CT17          | ---    | ---    | 1.26   | 1.23   | ---     | ---    | ---    | ---    |
| CT1           | ---    | ---    | ---    | 1.12   | 1.245   | ---    | ---    | ---    |
| CT4           | ---    | ---    | 1.03   | 1.25   | 1.535   | ---    | ---    | ---    |
| CT5           | ---    | ---    | ---    | 1.34   | 1.975   | ---    | ---    | ---    |
| CT6           | ---    | ---    | 1.00   | 1.06   | 1.575   | ---    | ---    | ---    |
| CT11          | 1.16   | ---    | 1.25   | 1.80   | 2.285   | ---    | ---    | ---    |

Table 9B

ΔCt values in lung and colon primary tumors and cell line models

| Primary Tumor | PRO943 | PRO1005 | PRO1009 | PRO1185 | PRO1245 | PRO1097 | PRO1107 | PRO1111 | PRO1153 |
|---------------|--------|---------|---------|---------|---------|---------|---------|---------|---------|
| LT-1          | ---    | 1.07    | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
| LT-1a         | ---    | 3.87    | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
| LT2           | ---    | ---     | ---     | ---     | ---     | 1.23    | ---     | ---     | ---     |
| LT3           | ---    | 1.61    | ---     | 1.01    | ---     | ---     | ---     | 1.39    | ---     |
| LT4           | ---    | ---     | ---     | ---     | ---     | ---     | ---     | 1.49    | 1.01    |
| LT6           | ---    | 1.29    | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
| LT7           | ---    | ---     | ---     | ---     | ---     | ---     | ---     | 1.58    | 1.52    |
| LT9           | ---    | 2.50    | ---     | ---     | ---     | 1.21    | ---     | 1.44    | ---     |
| LT10          | ---    | ---     | ---     | ---     | ---     | ---     | ---     | 1.05    | ---     |
| LT11          | 2.06   | ---     | ---     | ---     | ---     | ---     | ---     | 1.45    | ---     |
| LT12          | 1.94   | 1.21    | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
| LT13          | 1.64   | 2.30    | ---     | ---     | 3.84    | ---     | 3.55    | ---     | ---     |
| LT15          | 2.05   | 1.03    | ---     | ---     | 1.01    | ---     | 2.47    | ---     | ---     |
| LT16          | ---    | 1.05    | ---     | ---     | 1.98    | ---     | 2.45    | ---     | ---     |
| LT17          | 1.93   | ---     | ---     | ---     | ---     | ---     | ---     | 1.47    | ---     |
| LT19          | 2.90   | ---     | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
| LT26          | ---    | ---     | ---     | 1.66    | ---     | ---     | ---     | ---     | ---     |
| LT30          | ---    | ---     | ---     | 1.58    | ---     | ---     | ---     | ---     | ---     |
| CT2           | 1.92   | ---     | 2.00    | 1.73    | ---     | ---     | 4.75    | ---     | ---     |
| CT3           | 1.70   | ---     | 1.75    | ---     | ---     | ---     | 1.52    | ---     | ---     |
| CT8           | 1.37   | ---     | 1.29    | ---     | ---     | ---     | ---     | ---     | ---     |
|               | 1.12   | ---     | ---     | ---     | ---     | ---     | ---     | ---     | ---     |

Table 9B (cont')  
 $\Delta$ Ct values in lung and colon primary tumors and cell line models

| Primary Tumor | PRO943 | PRO1005 | PRO1009 | PRO1185 | PRO1245 | PRO1097 | PRO1107 | PRO1111 | PRO1133 |
|---------------|--------|---------|---------|---------|---------|---------|---------|---------|---------|
| CT10          | 2.13   | ---     | 1.73    | ---     | ---     | ---     | 2.82    | ---     | ---     |
|               | 1.67   |         |         |         |         |         |         |         |         |
| CT12          | 1.43   | ---     | 1.92    | ---     | ---     | ---     | ---     | ---     | ---     |
| CT14          | 1.46   | ---     | 2.10    | ---     | ---     | 1.08    | 1.54    | 1.38    | ---     |
| CT15          | ---    | ---     | 2.02    | ---     | 1.00    | ---     | ---     | ---     | ---     |
| CT16          | ---    | ---     | 1.56    | ---     | ---     | 1.11    | ---     | ---     | ---     |
| CT17          | 1.30   | ---     | 1.76    | ---     | ---     | 1.34    | ---     | ---     | ---     |
| CT1           | 1.36   | ---     | ---     | ---     | ---     | ---     | 1.57    | ---     | ---     |
| CT4           | ---    | ---     | 1.06    | ---     | ---     | ---     | 1.59    | ---     | ---     |
| CT5           | 1.88   | ---     | 1.43    | ---     | ---     | ---     | ---     | ---     | ---     |
|               | 2.51   |         |         |         |         |         |         |         |         |
| CT6           | 1.41   | ---     | ---     | ---     | ---     | ---     | ---     | ---     | ---     |
|               | 1.75   |         |         |         |         |         |         |         |         |
| CT7           | ---    | ---     | ---     | ---     | ---     | ---     | ---     | 1.16    | ---     |
| CT11          | 2.80   | ---     | 1.83    | ---     | ---     | ---     | ---     | 1.17    | ---     |
|               | 2.61   |         |         |         |         |         |         |         |         |
| CT18          | 1.30   | ---     | ---     | ---     | ---     | ---     | ---     | 1.05    | ---     |
| HS22          | ---    | ---     | ---     | ---     | 1.10    | ---     | ---     | ---     | ---     |

Table 9C

 $\Delta$ Ct values in lung and colon primary tumors and cell line models

|    | Primary<br>Tumor | PRO1182 | PRO1184 | PRO1187 | PRO1281 |
|----|------------------|---------|---------|---------|---------|
| 5  | LT-1             | 1.81    | ---     | ---     | ---     |
|    | LT-1a            | ---     | 1.14    | ---     | ---     |
|    |                  |         | 1.09    |         |         |
| 10 | LT4              | 1.43    | 1.37    | ---     | ---     |
|    |                  |         | 1.18    |         |         |
|    | LT6              | ---     | 1.78    | ---     | ---     |
| 15 |                  |         | 1.66    |         |         |
|    |                  |         | 1.05    |         |         |
|    | LT9              | 1.43    | ---     | ---     | ---     |
| 20 | LT12             | ---     | 2.47    | 1.17    | ---     |
|    |                  |         | 2.61    |         |         |
|    |                  |         | 1.80    |         |         |
| 25 | LT15             | ---     | ---     | 1.55    | ---     |
|    | LT16             | ---     | 1.01    | 1.33    | ---     |
|    | LT17             | ---     | ---     | ---     | ---     |
| 30 | LT18             | ---     | 1.07    | ---     | ---     |
|    |                  |         | 1.13    |         |         |
|    | LT19             | ---     | 1.19    | ---     | ---     |
|    |                  |         | 1.35    |         |         |
|    |                  |         | 1.02    |         |         |
|    | LT21             | ---     | 1.00    | ---     | ---     |
|    |                  |         | 1.20    |         |         |
|    | CT2              | ---     | ---     | ---     | 1.15    |
|    | CT12             | ---     | ---     | ---     | 1.07    |

Because amplification of the various DNAs described above occurs in various cancerous tumors and tumor cell lines derived from various human tissues, these molecules likely play a significant role in tumor formation and/or growth. As a result, amplification and/or enhanced expression of these molecules can serve as a diagnostic for detecting the presence of tumor in an individual and antagonists (e.g., antibodies) directed against the proteins encoded by the above described DNA molecules would be expected to have utility in cancer therapy.

**EXAMPLE 171: Identification of Receptor/Ligand Interactions**

In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparation of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin). Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (e.g. Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (e.g. FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

Using these assays, the following receptor/ligand interactions have been herein identified:

- (1) PRO943 binds to FHF1, PRO183 (FHF2), PRO184 (FHF3) and PRO185 (FHF4) and vice versa.
- (2) PRO331 binds to PRO1133 and vice versa.
- (3) PRO363 binds to PRO1387 and vice versa.
- (4) PRO5723 binds to PRO1387 and vice versa.
- (5) PRO1114 binds to PRO3301 and PRO9940 and vice versa.
- (6) PRO9828 appears to be a novel fibroblast growth factor receptor (FGFR) ligand in that it binds to the known FGF receptors FGFR1, FGFR2IIIC, FGFR3IIIC and FGFR4. PRO9828 and agonists, therefore, will find use for activating the biological activities normally activated by FGF molecules including, for example, cell growth and proliferation. Antagonists of PRO9828 will find use in blocking the biological activities mediated through the FGF receptor.
- (7) PRO1181 binds to PRO7170, PRO361 and PRO846.

#### EXAMPLE 172: Tissue Expression Distribution

Oligonucleotide probes were constructed from the PRO polypeptide-encoding nucleotide sequences shown in the figures for use in quantitative PCR amplification reactions. The oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human adult and/or fetal tissue sources and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acids in the various tissues tested. Knowledge of the expression pattern or the differential expression of the PRO polypeptide-encoding nucleic acids in various different human tissue types provides a diagnostic marker useful for tissue typing, with or without other tissue-specific markers, for determining the primary tissue source of a metastatic tumor, disease diagnosis, and the like. These assays provided the following results.

| <u>DNA Molecule</u> | <u>Tissues w/ Significant Expression</u> | <u>Tissues w/o Significant Expression</u> |
|---------------------|--|---|
| DNA16422-1209       | substantia nigra, dendrocytes, uterus    | hippocampus                               |
| DNA16435-1208       | substantia nigra, dendrocytes, uterus    | hippocampus                               |
| DNA26843-1389       | dendrocytes, heart, uterus, colon tumor  | hippocampus, substantia nigra, cartilage  |

|    | <u>DNA Molecule</u> | <u>Tissues w/ Significant Expression</u>      | <u>Tissues w/o Significant Expression</u>                      |
|----|---------------------|---|--|
|    | DNA26844-1394       | HUVEC, dendrocytes, cartilage                 | substantia nigra, hippocampus, uterus, prostate                |
| 5  | DNA40621-1440       | prostate, uterus, colon tumor                 | brain, heart, HUVEC, cartilage                                 |
|    | DNA44161-1434       | colon tumor, dendrocytes                      | substantia nigra, hippocampus, prostate, uterus                |
| 10 | DNA44694-1500       | dendrocytes, hippocampus, prostate            | colon tumor, substantia nigra, heart                           |
|    | DNA48320-1433       | prostate, uterus                              | colon tumor, brain, heart, cartilage                           |
|    | DNA49647-1398       | brain, heart, prostate, uterus                | cartilage  |
|    | DNA53913-1490       | hippocampus                                   | substantia nigra, dendrocytes                                  |
| 15 | DNA53978-1443       | dendrocytes, uterus, prostate                 | substantia nigra, colon tumor                                  |
|    | DNA53996-1442       | spleen, prostate, uterus, hippocampus         | substantia nigra, heart  |
|    | DNA56050-1455       | prostate, uterus, cartilage, hippocampus      | heart, colon tumor, dendrocytes                                |
|    | DNA56110-1437       | spleen, colon tumor, brain, prostate          | heart  |
| 20 | DNA56410-1414       | uterus, dendrocytes                           | hippocampus, substantia nigra, heart                           |
|    | DNA56436-1448       | substantia nigra, prostate, hippocampus       | dendrocytes, heart, HUVEC                                      |
|    | DNA56855-1447       | prostate, uterus                              | brain, cartilage, heart, colon tumor                           |
|    | DNA56860-1510       | colon tumor                                   | prostate, uterus, dendrocytes                                  |
| 25 | DNA56868-1478       | colon tumor, prostate                         | uterus, brain, heart, cartilage                                |
|    | DNA56869-1545       | prostate, uterus, cartilage                   | brain, colon tumor, spleen, heart                              |
|    | DNA57699-1412       | dendrocytes, hippocampus, prostate            | substantia nigra, heart  |
|    | DNA57704-1452       | brain, heart, spleen, uterus, prostate        | colon tumor  |
| 30 | DNA57710-1451       | dendrocytes, hippocampus, spleen, uterus      | substantia nigra, heart  |
|    | DNA57711-1501       | dendrocytes, hippocampus, heart, cartilage    | substantia nigra   |
|    | DNA57827-1493       | colon tumor, hippocampus, prostate            | substantia nigra, dendrocytes, uterus                          |
|    | DNA58723-1588       | substantia nigra, cartilage uterus            | hippocampus, dendrocytes, HUVEC                                |
| 35 | DNA58743-1609       | brain, prostate, uterus                       | colon tumor, heart, spleen, cartilage                          |
|    | DNA58846-1409       | hippocampus, dendrocytes                      | substantia nigra, uterus, prostate, colon tumor                |
|    | DNA58849-1494       | prostate                                      | brain, uterus, cartilage, heart, colon tumor                   |
|    | DNA58850-1495       | spleen, prostate, dendrocytes                 | hippocampus, substantia nigra, colon tumor                     |
| 40 | DNA59213-1487       | spleen, cartilage, prostate, substantia nigra | heart, hippocampus, dendrocytes                                |
|    | DNA59497-1496       | dendrocytes, prostate, uterus, heart          | cartilage, hippocampus, substantia nigra                       |
|    | DNA59605-1418       | dendrocytes, prostate, uterus                 | hippocampus, substantia nigra, colon tumor                     |
|    | DNA59609-1470       | dendrocytes                                   | substantia nigra, hippocampus, heart, prostate, uterus, spleen |
| 45 | DNA59612-1466       | prostate, dendrocytes                         | hippocampus, substantia nigra, uterus, colon tumor             |
|    | DNA59616-1465       | dendrocytes, substantia nigra, colon tumor    | hippocampus  |
|    | DNA59619-1464       | dendrocytes, substantia nigra, colon tumor    | hippocampus  |
|    | DNA59625-1498       | brain, colon tumor, prostate, uterus          | THP-1 macrophages  |
| 50 | DNA59827-1426       | substantia nigra, prostate, uterus            | hippocampus, dendrocytes, heart                                |
|    | DNA59828-1608       | dendrocytes, substantia nigra, colon tumor    | hippocampus  |
|    | DNA59853-1505       | prostate                                      | brain, uterus, spleen, heart, colon tumor                      |
|    | DNA59854-1459       | cartilage                                     | prostate, brain, heart, colon tumor                            |
| 55 | DNA60283-1484       | dendrocytes, spleen, prostate, uterus         | hippocampus, substantia nigra, heart                           |
|    | DNA60619-1482       | dendrocytes, substantia nigra, colon tumor    | hippocampus  |
|    | DNA60625-1507       | cartilage                                     | prostate, brain, heart, colon tumor                            |
|    | DNA60629-1481       | uterus, colon tumor, substantia nigra         | hippocampus, dendrocytes, spleen, prostate                     |
|    | DNA61755-1554       | dendrocytes, substantia nigra, colon tumor    | hippocampus  |

| <u>DNA Molecule</u> | <u>Tissues w/ Significant Expression</u>                       | <u>Tissues w/o Significant Expression</u> |
|---------------------|--|---|
| DNA64852-1589       | prostate, uterus   | brain, heart, cartilage, colon tumor      |
| DNA66308-1537       | prostate, heart uterus   | brain, colon tumor, cartilage             |
| DNA68869-1610       | spleen, prostate, heart, uterus, colon tumor, substantia nigra | hippocampus, dendrocytes, prostate        |

5

EXAMPLE 173: Isolation of cDNA Clones Encoding Human PRO846

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39949. Based on the DNA39949 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO846.

10

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCCTGCAGTGCACCTACAGGGAAG-3' (SEQ ID NO:518)

reverse PCR primer 5'-CTGTCTTCCCTGCTTGGCTGTGG-3' (SEQ ID NO:519)

15

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39949 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGCAGGAAGGGTGGGATCCTCTTCTCTCGCTGCTCTGGCCACATC-3'

(SEQ ID NO:520)

20

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO846 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO846 [herein designated as DNA44196-1353] (SEQ ID NO:516) and the derived protein sequence for PRO846.

25

The entire nucleotide sequence of UNQ422 (DNA44196-1353) is shown in Figure 329 (SEQ ID NO:516). Clone UNQ422 (DNA44196-1353) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon at nucleotide positions 1021-1023 (Figure 329). The predicted polypeptide precursor is 332 amino acids long (Figure 330). The full-length PRO846 protein shown in Figure 330 has an estimated molecular weight of about 36,143 daltons and a pI of about 5.89. Important regions of the amino acid sequence of PRO846 include the signal peptide, the transmembrane domain, an N-glycosylation site, a sequence typical of fibrinogen beta and gamma chains C-terminal domain, and a sequence typical of Ig like V-type domain as shown in Figure 330. Clone UNQ422 (DNA44196-1353) has been deposited with ATCC and is assigned ATCC deposit no. 209847.

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**EXAMPLE 174: Isolation of cDNA Clones Encoding Human PRO363**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42828. Based on the DNA42828 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO363.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (42828.f1) 5'-CCAGTGCACAGCAGGCAACGAAGC-3' (SEQ ID NO:521)

reverse PCR primer (42828.r1) 5'-ACTAGGCTGTATGCCTGGGTGGGC-3' (SEQ ID NO:522)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42828 sequence which had the following nucleotide sequence

hybridization probe (42828.p1)

5'-GTATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGC-3' (SEQ ID NO:523)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO363 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO363 [herein designated as UNQ318 (DNA45419-1252)] (SEQ ID NO:500) and the derived protein sequence for PRO363.

The entire nucleotide sequence of UNQ318 (DNA45419-1252) is shown in Figure 313 (SEQ ID NO:500). Clone UNQ318 (DNA45419-1252) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 190-192 and ending at the stop codon at nucleotide positions 1309-1311 (Figure 313). The predicted polypeptide precursor is 373 amino acids long (Figure 314). The full-length PRO363 protein shown in Figure 314 has an estimated molecular weight of about 41,281 daltons and a pI of about 8.33. A transmembrane domain exists at amino acids 221 to 254 of the amino acid sequence shown in Figure 314 (SEQ ID NO:501). The PRO363 polypeptide also possesses at least two myelin P0 protein domains from about amino acids 15 to 56 and from about amino acids 87 to 116. Clone UNQ318 (DNA45419-1252) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209616.

Analysis of the amino acid sequence of the full-length PRO363 polypeptide suggests that it possesses significant sequence similarity to the cell surface protein HCAR, thereby indicating that PRO363 may be a novel HCAR homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO363 amino acid sequence and the following Dayhoff sequences, HS46KDA\_1, HSU90716\_1, MMCARH\_1, MMCARHOM\_1, MMU90715\_1, A33\_HUMAN, P\_W14146, P\_W14158, A42632 and B42632.

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**EXAMPLE 175: Isolation of cDNA Clones Encoding a Human PRO9828**

A consensus DNA sequence was assembled relative to other nucleic sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA139814. Based on the DNA139814 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO9828. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

5'-AATCTCAGCACCAGCCACTCAGAGCA-3' (SEQ ID NO:524)

5'-GTAAAGAGGGTGCCCTTCCAGCGA-3' (SEQ ID NO:525)

5'-TATCCCAATGCCTCCCCACTGCTC-3' (SEQ ID NO:526)

5'-GATGAAGTGGCGAAGGGGCGGCA-3' (SEQ ID NO:527)

RNA for construction of the cDNA libraries was isolated from human fetal liver tissue. The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for a full-length PRO9828 polypeptide (designated herein as DNA142238-2768 [Figure 323, SEQ ID NO:510]) and the derived protein sequence for that PRO9828 polypeptide.

The full length clone identified above contained a single open reading frame with an apparent translational initiation site at nucleotide positions 232-234 and a stop signal at nucleotide positions 985-987 (Figure 323, SEQ ID NO:510). The predicted polypeptide precursor is 251 amino acids long, has a calculated molecular weight of approximately 27,954 daltons and an estimated pI of approximately 9.22. Analysis of the full-length PRO9828 sequence shown in Figure 324 (SEQ ID NO:511) evidences the presence of a variety of important polypeptide domains as shown in Figure 324, wherein the locations given for those important polypeptide domains are approximate as described above. Chromosome mapping evidences that the PRO9828-encoding nucleic acid maps to chromosome 12p13 in humans. Clone DNA142238-2768 has been deposited with ATCC on October 5, 1999 and is assigned ATCC deposit no. 819-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 324 (SEQ ID NO:511), evidenced sequence

identity between the PRO9828 amino acid sequence and the following Dayhoff sequences: P\_Y08581, AB018122\_1, FGF3\_HUMAN, P\_R70824, S54407, P\_R80780, P\_Y23761, P\_W92312, OMFGF6\_1 and P\_R80871.

EXAMPLE 176: Isolation of cDNA Clones Encoding a Human PRO7170

5 DNA108722-2743 was identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., Genbank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals.

Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, designated herein as CLU57836. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., Genbank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58756.

In light of an observed sequence homology between the DNA58756 sequence and an EST sequence encompassed within clone no. 2251462 from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, clone no. 2251462 was purchased and the cDNA insert was obtained and sequenced. It was found herein that that cDNA insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 325 and is herein designated as DNA108722-2743.

Clone DNA108722-2743 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon at nucleotide positions 1506-1508 (Figure 325). The predicted polypeptide precursor is 482 amino acids long (Figure 326). The full-length PRO7170 protein shown in Figure 326 has an estimated molecular weight of about 49,060 daltons and a pI of about 4.74. Analysis of the full-length PRO7170 sequence shown in Figure 326 (SEQ ID NO:513) evidences the presence of a variety of important polypeptide domains as shown in Figure 326, wherein the locations given for those important polypeptide domains are approximate as described above. Clone DNA108722-2743 has been

deposited with ATCC on August 17, 1999 and is assigned ATCC Deposit No. 552-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 326 (SEQ ID NO:513), evidenced sequence identity between the PRO7170 amino acid sequence and the following Dayhoff sequences: P\_Y12291, I47141, D88733\_1, DMC56G7\_1, P\_Y11606, HWPI\_CANAL, HSMUC5BEX\_1, HSU78550\_1, HSU70136\_1, and  
5 SGS3\_DROME.

#### EXAMPLE 177: Isolation of cDNA Clones Encoding Human PRO361

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40654. Based on the DNA40654  
10 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO361.

Forward and reverse PCR primers were synthesized as follows:

|                           |                                      |                 |
|---------------------------|--------------------------------------|-----------------|
| <u>forward PCR primer</u> | 5'-AGGGAGGATTATCCTTGACCTTTGAAGACC-3' | (SEQ ID NO:528) |
| <u>forward PCR primer</u> | 5'-GAAGCAAGTGCCAGCTC-3'              | (SEQ ID NO:529) |
| <u>forward PCR primer</u> | 5'-CGGGTCCCTGCTCTTTGG-3'             | (SEQ ID NO:530) |
| <u>reverse PCR primer</u> | 5'-CACCGTAGCTGGGAGCGCACTCAC-3'       | (SEQ ID NO:531) |
| <u>reverse PCR primer</u> | 5'-AGTGTAAGTCAAGCTCCC-3'             | (SEQ ID NO:532) |

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus  
20 DNA40654 sequence which had the following nucleotide sequence

#### hybridization probe

5'- GCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATTGCCTCAAAAAGAG-3' (SEQ ID NO:533)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then  
25 used to isolate clones encoding the PRO361 gene using the probe oligonucleotide. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO361 [herein designated as DNA45410-1250] (SEQ ID NO:514) and the derived protein sequence for PRO361.

The entire nucleotide sequence of DNA45410-1250 is shown in Figure 327 (SEQ ID NO:514). Clone DNA45410-1250 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 226-228 and ending at the stop codon at nucleotide positions 1519-1521 (Figure 327). The predicted polypeptide precursor is 431 amino acids long (Figure 328). The full-length PRO361 protein shown in Figure 328 has an estimated molecular weight of about 46,810 daltons and a pI of about 6.45. In addition, regions  
35 of interest including the transmembrane domain (amino acids 380-409) and sequences typical of the arginase family of proteins (amino acids 3-14 and 39-57) are designated in Figure 328. Clone DNA45410-1250 has been deposited with ATCC and is assigned ATCC deposit no. ATCC 209621.

Analysis of the amino acid sequence of the full-length PRO361 polypeptide suggests that portions of it possess significant homology to the mucin and/or chitinase proteins, thereby indicating that PRO361 may be a novel mucin and/or chitinase protein.

EXAMPLE 178: Isolation of cDNA Clones Encoding a Human PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940

DNA molecules encoding the PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940 polypeptides shown in the accompanying figures were obtained through GenBank.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 10

|    | <u>Material</u> | <u>ATCC Dep. No.</u> | <u>Deposit Date</u> |
|----|-----------------|----------------------|---------------------|
| 15 | DNA45410-1250   | 209621               | February 5, 1998    |
|    | DNA108722-2743  | 552-PTA              | August 17, 1999     |
|    | DNA142238-2768  | 819-PTA              | October 5, 1999     |
|    | DNA40981-1234   | 209439               | November 7, 1997    |
|    | DNA45419-1252   | 209616               | February 5, 1998    |
| 20 | DNA44196-1353   | 209847               | May 6, 1998         |
|    | DNA16422-1209   | 209929               | June 2, 1998        |
|    | DNA16435-1208   | 209930               | June 2, 1998        |
|    | DNA21624-1391   | 209917               | June 2, 1998        |
|    | DNA23334-1392   | 209918               | June 2, 1998        |
| 25 | DNA26288-1239   | 209792               | April 21, 1998      |
|    | DNA26843-1389   | 203099               | August 4, 1998      |
|    | DNA26844-1394   | 209926               | June 2, 1998        |
|    | DNA30862-1396   | 209920               | June 2, 1998        |
|    | DNA35680-1212   | 209790               | April 21, 1998      |
| 30 | DNA40621-1440   | 209922               | June 2, 1998        |
|    | DNA44161-1434   | 209907               | May 27, 1998        |
|    | DNA44694-1500   | 203114               | August 11, 1998     |
|    | DNA45495-1550   | 203156               | August 25, 1998     |
|    | DNA47361-1154   | 209431               | November 7, 1997    |
| 35 | DNA47394-1572   | 203109               | August 11, 1998     |
|    | DNA48320-1433   | 209904               | May 27, 1998        |
|    | DNA48334-1435   | 209924               | June 2, 1998        |
|    | DNA48606-1479   | 203040               | July 1, 1998        |
|    | DNA49141-1431   | 203003               | June 23, 1998       |
| 40 | DNA49142-1430   | 203002               | June 23, 1998       |
|    | DNA49143-1429   | 203013               | June 23, 1998       |
|    | DNA49647-1398   | 209919               | June 2, 1998        |
|    | DNA49819-1439   | 209931               | June 2, 1998        |
|    | DNA49820-1427   | 209932               | June 2, 1998        |
| 45 | DNA49821-1562   | 209981               | June 16, 1998       |
|    | DNA52192-1369   | 203042               | July 1, 1998        |
|    | DNA52598-1518   | 203107               | August 11, 1998     |
|    | DNA53913-1490   | 203162               | August 25, 1998     |

Table 10 (cont')

|    |               |        |                 |
|----|---------------|--------|-----------------|
|    | DNA53978-1443 | 209983 | June 16, 1998   |
|    | DNA53996-1442 | 209921 | June 2, 1998    |
|    | DNA56041-1416 | 203012 | June 23, 1998   |
| 5  | DNA56047-1456 | 209948 | June 9, 1998    |
|    | DNA56050-1455 | 203011 | June 23, 1998   |
|    | DNA56110-1437 | 203113 | August 11, 1998 |
|    | DNA56113-1378 | 203049 | July 1, 1998    |
|    | DNA56410-1414 | 209923 | June 2, 1998    |
| 10 | DNA56436-1448 | 209902 | May 27, 1998    |
|    | DNA56855-1447 | 203004 | June 23, 1998   |
|    | DNA56859-1445 | 203019 | June 23, 1998   |
|    | DNA56860-1510 | 209952 | June 9, 1998    |
|    | DNA56865-1491 | 203022 | June 23, 1998   |
| 15 | DNA56866-1342 | 203023 | June 23, 1998   |
|    | DNA56868-1209 | 203024 | June 23, 1998   |
|    | DNA56869-1545 | 203161 | August 25, 1998 |
|    | DNA56870-1492 | 209925 | June 2, 1998    |
|    | DNA57033-1403 | 209905 | May 27, 1998    |
|    | DNA57037-1444 | 209903 | May 27, 1998    |
| 20 | DNA57129-1413 | 209977 | June 16, 1998   |
|    | DNA57690-1374 | 209950 | June 9, 1998    |
|    | DNA57693-1424 | 203008 | June 23, 1998   |
|    | DNA57694-1341 | 203017 | June 23, 1998   |
| 25 | DNA57695-1340 | 203006 | June 23, 1998   |
|    | DNA57699-1412 | 203020 | June 23, 1998   |
|    | DNA57702-1476 | 209951 | June 9, 1998    |
|    | DNA57704-1452 | 209953 | June 9, 1998    |
|    | DNA57708-1411 | 203021 | June 23, 1998   |
|    | DNA57710-1451 | 203048 | July 1, 1998    |
| 30 | DNA57711-1501 | 203047 | July 1, 1998    |
|    | DNA57827-1493 | 203045 | July 1, 1998    |
|    | DNA57834-1339 | 209954 | June 9, 1998    |
|    | DNA57836-1338 | 203025 | June 23, 1998   |
|    | DNA57838-1337 | 203014 | June 23, 1998   |
| 35 | DNA57844-1410 | 203010 | June 23, 1998   |
|    | DNA58721-1475 | 203110 | August 11, 1998 |
|    | DNA58723-1588 | 203133 | August 18, 1998 |
|    | DNA58737-1473 | 203136 | August 18, 1998 |
| 40 | DNA58743-1609 | 203154 | August 25, 1998 |
|    | DNA58846-1409 | 209957 | June 9, 1998    |
|    | DNA58848-1472 | 209955 | June 9, 1998    |
|    | DNA58849-1494 | 209958 | June 9, 1998    |
|    | DNA58850-1495 | 209956 | June 9, 1998    |
| 45 | DNA58853-1423 | 203016 | June 23, 1998   |
|    | DNA58855-1422 | 203018 | June 23, 1998   |
|    | DNA59205-1421 | 203009 | June 23, 1998   |
|    | DNA59211-1450 | 209960 | June 9, 1998    |
|    | DNA59213-1487 | 209959 | June 9, 1998    |
|    | DNA59214-1449 | 203046 | July 1, 1998    |
| 50 | DNA59215-1425 | 209961 | June 9, 1998    |
|    | DNA59220-1514 | 209962 | June 9, 1998    |
|    | DNA59488-1603 | 203157 | August 25, 1998 |
|    | DNA59493-1420 | 203050 | July 1, 1998    |
|    | DNA59497-1496 | 209941 | June 4, 1998    |
| 55 | DNA59588-1571 | 203106 | August 11, 1998 |

Table 10 (cont')

|    |               |        |                    |
|----|---------------|--------|--------------------|
|    | DNA59603-1419 | 209944 | June 9, 1998       |
|    | DNA59605-1418 | 203005 | June 23, 1998      |
|    | DNA59606-1471 | 209945 | June 9, 1998       |
| 5  | DNA59607-1497 | 209957 | June 9, 1998       |
|    | DNA59609-1470 | 209963 | June 9, 1998       |
|    | DNA59610-1559 | 209990 | June 16, 1998      |
|    | DNA59612-1466 | 209947 | June 9, 1998       |
|    | DNA59613-1417 | 203007 | June 23, 1998      |
| 10 | DNA59616-1465 | 209991 | June 16, 1998      |
|    | DNA59619-1464 | 203041 | July 1, 1998       |
|    | DNA59620-1463 | 209989 | June 16, 1998      |
|    | DNA59625-1498 | 209992 | June 17, 1998      |
|    | DNA59767-1489 | 203108 | August 11, 1998    |
|    | DNA59776-1600 | 203128 | August 18, 1998    |
| 15 | DNA59777-1480 | 203111 | August 11, 1998    |
|    | DNA59820-1549 | 203129 | August 18, 1998    |
|    | DNA59827-1426 | 203089 | August 4, 1998     |
|    | DNA59828-1608 | 203158 | August 25, 1998    |
| 20 | DNA59838-1462 | 209976 | June 16, 1998      |
|    | DNA59839-1461 | 209988 | June 16, 1998      |
|    | DNA59841-1460 | 203044 | July 1, 1998       |
|    | DNA59842-1502 | 209982 | June 16, 1998      |
|    | DNA59846-1503 | 209978 | June 16, 1998      |
| 25 | DNA59847-1511 | 203098 | August 4, 1998     |
|    | DNA59848-1512 | 203088 | August 4, 1998     |
|    | DNA59849-1504 | 209986 | June 16, 1998      |
|    | DNA59853-1505 | 209985 | June 16, 1998      |
|    | DNA59854-1459 | 209974 | June 16, 1998      |
| 30 | DNA60283-1484 | 203043 | July 1, 1998       |
|    | DNA60615-1483 | 209980 | June 16, 1998      |
|    | DNA60619-1482 | 209993 | June 16, 1998      |
|    | DNA60621-1516 | 203091 | August 4, 1998     |
|    | DNA60622-1525 | 203090 | August 4, 1998     |
| 35 | DNA60625-1507 | 209975 | June 16, 1998      |
|    | DNA60627-1508 | 203092 | August 4, 1998     |
|    | DNA60629-1481 | 209979 | June 16, 1998      |
|    | DNA61755-1554 | 203112 | August 11, 1998    |
|    | DNA61873-1574 | 203132 | August 18, 1998    |
| 40 | DNA62814-1521 | 203093 | August 4, 1998     |
|    | DNA62872-1509 | 203100 | August 4, 1998     |
|    | DNA62876-1517 | 203095 | August 4, 1998     |
|    | DNA62881-1515 | 203096 | August 4, 1998     |
|    | DNA64852-1589 | 203127 | August 18, 1998    |
| 45 | DNA64884-1527 | 203155 | August 25, 1998    |
|    | DNA64890-1612 | 203131 | August 18, 1998    |
|    | DNA65412-1523 | 203094 | August 4, 1998     |
|    | DNA66308-1537 | 203159 | August 25, 1998    |
|    | DNA66309-1538 | 203235 | September 15, 1998 |
| 50 | DNA67004-1614 | 203115 | August 11, 1998    |
|    | DNA68869-1610 | 203164 | August 25, 1998    |
|    | DNA68872-1620 | 203160 | August 25, 1998    |
|    | DNA71159-1617 | 203135 | August 18, 1998    |

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.



WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28),  
5 Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure  
10 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure  
20 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure  
30 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure  
35 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure

284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID

NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure

181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 10.
5. A vector comprising the nucleic acid of Claim 1.
6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
7. A host cell comprising the vector of Claim 5.
8. The host cell of Claim 7 wherein said cell is a CHO cell.
9. The host cell of Claim 7 wherein said cell is an *E. coli*.
10. The host cell of Claim 7 wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID

NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 10.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

20. The antibody of Claim 17 wherein said antibody is an antibody fragment.

21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50

(SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46),  
5 Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure  
10 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure  
15 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure  
20 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure  
25 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure  
30 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure  
35 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure



293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

23. An isolated extracellular domain of of PRO polypeptide.

24. An isolated PRO polypeptide lacking its associated signal peptide.

25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.

26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

27. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure

169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID

NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure

90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

28. An isolated polypeptide having at least 80% amino acid sequence identity to:
- (a) the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36),

Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID

NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID

NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure

254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

29. A method of detecting a PRO943 polypeptide in a sample suspected of containing a PRO943 polypeptide, said method comprising contacting said sample with a PRO183, PRO184 or PRO185 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO943 polypeptide in said sample.

30. The method according to Claim 29, wherein said sample comprises cells suspected of expressing said PRO943 polypeptide.

31. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is labeled with a detectable label.

32. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is attached to a solid support.

33. A method of detecting a PRO183, PRO184 or PRO185 polypeptide in a sample suspected of containing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said sample with a PRO943 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO183, PRO184 or PRO185 polypeptide in said sample.

34. The method according to Claim 33, wherein said sample comprises cells suspected of expressing said PRO183, PRO184 or PRO185 polypeptide.



35. The method according to Claim 33, wherein said PRO943 polypeptide is labeled with a detectable label.

36. The method according to Claim 33, wherein said PRO943 polypeptide is attached to a solid support.

37. A method of detecting a PRO331 polypeptide in a sample suspected of containing a PRO331 polypeptide, said method comprising contacting said sample with a PRO1133 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO331 polypeptide in said sample.

38. The method according to Claim 37, wherein said sample comprises cells suspected of expressing said PRO331 polypeptide.

39. The method according to Claim 37, wherein said PRO1133 polypeptide is labeled with a detectable label.

40. The method according to Claim 37, wherein said PRO1133 polypeptide is attached to a solid support.

41. A method of detecting a PRO1133 polypeptide in a sample suspected of containing a PRO1133 polypeptide, said method comprising contacting said sample with a PRO331 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1133 polypeptide in said sample.

42. The method according to Claim 41, wherein said sample comprises cells suspected of expressing said PRO1133 polypeptide.

43. The method according to Claim 41, wherein said PRO331 polypeptide is labeled with a detectable label.

44. The method according to Claim 41, wherein said PRO331 polypeptide is attached to a solid support.

45. A method of detecting a PRO363 or PRO5723 polypeptide in a sample suspected of containing a PRO363 or PRO5723 polypeptide, said method comprising contacting said sample with a PRO1387 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO363

or PRO5723 polypeptide in said sample.

46. The method according to Claim 45, wherein said sample comprises cells suspected of expressing said PRO363 or PRO5723 polypeptide.

5 47. The method according to Claim 45, wherein said PRO1387 polypeptide is labeled with a detectable label.

48. The method according to Claim 45, wherein said PRO1387 polypeptide is attached to a solid support.

10 49. A method of detecting a PRO1387 polypeptide in a sample suspected of containing a PRO1387 polypeptide, said method comprising contacting said sample with a PRO363 or PRO5723 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1387 polypeptide in said sample.

15 50. The method according to Claim 49, wherein said sample comprises cells suspected of expressing said PRO1387 polypeptide.

20 51. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is labeled with a detectable label.

52. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is attached to a solid support.

25 53. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO3301 or PRO9940 polypeptide and determining the formation of a PRO1114/PRO3301 or PRO9940 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

30 54. The method according to Claim 53, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

35 55. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is labeled with a detectable label.

56. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is attached to a solid support.

57. A method of detecting a PRO3301 or PRO9940 polypeptide in a sample suspected of containing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO3301 or PRO9940/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO3301 or PRO9940 polypeptide in said sample.

58. The method according to Claim 57, wherein said sample comprises cells suspected of expressing said PRO3301 or PRO9940 polypeptide.

59. The method according to Claim 57, wherein said PRO1114 polypeptide is labeled with a detectable label.

60. The method according to Claim 57, wherein said PRO1114 polypeptide is attached to a solid support.

61. A method of detecting a PRO1181 polypeptide in a sample suspected of containing a PRO1181 polypeptide, said method comprising contacting said sample with a PRO7170, PRO361 or PRO846 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1181 polypeptide in said sample.

62. The method according to Claim 61, wherein said sample comprises cells suspected of expressing said PRO1181 polypeptide.

63. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is labeled with a detectable label.

64. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is attached to a solid support.

65. A method of detecting a PRO7170, PRO361 or PRO846 polypeptide in a sample suspected of containing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said sample with a PRO1181 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO7170, PRO361 or PRO846 polypeptide in said sample.

66. The method according to Claim 65, wherein said sample comprises cells suspected of expressing said PRO7170, PRO361 or PRO846 polypeptide.

67. The method according to Claim 65, wherein said PRO1181 polypeptide is labeled with a detectable label.

68. The method according to Claim 65, wherein said PRO1181 polypeptide is attached to a solid support.

69. A method of linking a bioactive molecule to a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

70. The method according to Claim 69, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

71. The method according to Claim 69, wherein said bioactive molecule causes the death of said cell.

72. A method of linking a bioactive molecule to a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

73. The method according to Claim 72, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

74. The method according to Claim 73, wherein said bioactive molecule causes the death of said cell.

75. A method of linking a bioactive molecule to a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

76. The method according to Claim 75, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

77. The method according to Claim 75, wherein said bioactive molecule causes the death of said cell.

78. A method of linking a bioactive molecule to a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

79. The method according to Claim 78, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

80. The method according to Claim 78, wherein said bioactive molecule causes the death of said cell.

81. A method of linking a bioactive molecule to a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

82. The method according to Claim 81, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

83. The method according to Claim 81, wherein said bioactive molecule causes the death of said cell.

84. A method of linking a bioactive molecule to a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

85. The method according to Claim 84, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

86. The method according to Claim 84, wherein said bioactive molecule causes the death of said cell.

87. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

5 88. The method according to Claim 87, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

89. The method according to Claim 87, wherein said bioactive molecule causes the death of said cell.

10

90. A method of linking a bioactive molecule to a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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91. The method according to Claim 90, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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92. The method according to Claim 90, wherein said bioactive molecule causes the death of said cell.

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93. A method of linking a bioactive molecule to a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

94. The method according to Claim 93, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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95. The method according to Claim 93, wherein said bioactive molecule causes the death of said cell.

35

96. A method of linking a bioactive molecule to a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

97. The method according to Claim 96, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

98. The method according to Claim 96, wherein said bioactive molecule causes the death of said cell.

99. A method of modulating at least one biological activity of a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide or an anti-PRO943 antibody, whereby said PRO183, PRO184 or PRO185 polypeptide or said anti-PRO943 antibody binds to said PRO943 polypeptide, thereby modulating at least one biological activity of said cell.

100. The method according to Claim 99, wherein said cell is killed.

101. A method of modulating at least one biological activity of a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide or an anti-PRO183, anti-PRO184 or anti-PRO185 antibody, whereby said PRO943 polypeptide or said anti-PRO183, anti-PRO184 or anti-PRO185 antibody binds to said PRO183, PRO184 or PRO185 polypeptide, thereby modulating at least one biological activity of said cell.

102. The method according to Claim 101, wherein said cell is killed.

103. A method of modulating at least one biological activity of a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide or an anti-PRO331 antibody, whereby said PRO1133 polypeptide or said anti-PRO331 antibody binds to said PRO331 polypeptide, thereby modulating at least one biological activity of said cell.

104. The method according to Claim 103, wherein said cell is killed.

105. A method of modulating at least one biological activity of a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide or an anti-PRO1133 antibody, whereby said PRO331 polypeptide or said anti-PRO1133 antibody binds to said PRO1133 polypeptide, thereby modulating at least one biological activity of said cell.

106. The method according to Claim 105, wherein said cell is killed.

107. A method of modulating at least one biological activity of a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide or an anti-PRO1387 antibody, whereby said PRO363 or PRO5723 polypeptide or said anti-PRO1387 antibody binds to said PRO1387 polypeptide, thereby modulating at least one biological activity of said cell.

5 108. The method according to Claim 107, wherein said cell is killed.

109. A method of modulating at least one biological activity of a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide or an anti-PRO363 or anti-PRO5723 antibody, whereby said PRO1387 polypeptide or said anti-PRO363 or anti-PRO5723 antibody binds to said PRO363 or PRO5723 polypeptide, thereby modulating at least one biological activity of said cell.

110. The method according to Claim 109, wherein said cell is killed.

15 111. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide or an anti-PRO1114 antibody, whereby said PRO3301 or PRO9940 polypeptide or said anti-PRO1114 antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.

20 112. The method according to Claim 111, wherein said cell is killed.

113. A method of modulating at least one biological activity of a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO3301 or anti-PRO9940 antibody, whereby said PRO1114 polypeptide or said anti-PRO3301 or anti-PRO9940 antibody binds to said PRO3301 or PRO9940 polypeptide, thereby modulating at least one biological activity of said cell.

114. The method according to Claim 113, wherein said cell is killed.

30 115. A method of modulating at least one biological activity of a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide or an anti-PRO1181 antibody, whereby said PRO7170, PRO361 or PRO846 polypeptide or said anti-PRO1181 antibody binds to said PRO1181 polypeptide, thereby modulating at least one biological activity of said cell.

35 116. The method according to Claim 115, wherein said cell is killed.



117. A method of modulating at least one biological activity of a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide or an anti-PRO7170, anti-PRO361 or anti-PRO846 antibody, whereby said PRO1181 polypeptide or said anti-PRO7170, anti-PRO361 or anti-PRO846 antibody binds to said PRO7170, PRO361 or PRO846 polypeptide, thereby modulating at least one biological activity of said cell.

5

118. The method according to Claim 117, wherein said cell is killed.

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**FIGURE 1**

CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTTCAGATCTGCTCGGTTAGA  
CCTGGTGCACCACCACC**ATG**TGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG  
GTTTTCCACCCAGCTTTCACCAAGGCCTCCCCTGTTGTGAAGAATTCATCACGAAGAATCA  
ATGGCTGTTAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA  
GAACTGGCCAAGAAGCTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATATTTAAAATT  
GATCAGATGGGAAGATGGTTTGTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA  
CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT  
ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAACAGCT  
TTGTCTGCCATAGCAATCAGCAGAACGCCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG  
GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC  
CATATGACCAGAGCCCAGGCCCAAAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT  
GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCTCTTCTCATCAGAGCTGCATGGTACAC  
AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCAGTGAAAAGTTTCTGA  
ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCCTCATTGGGATCTATG  
TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT  
AGTTCTTTTCAGCATGTTCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT  
CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACTCGATGCTGAGTATCTACATGGAT  
ACATTAAATATATTTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAGAA**TG**  
**A**AGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC  
ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA  
TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT  
AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT  
TTGGTGAATGTGAAAACATAAGTTTGTGTCATGAGAATGTAAGTCTTTTTTCTACTTTAAAA  
TTTAGTAGGTTCACTGAGTAACTAAAATTTAGCAAACTGTGTTTGCATATTTTTTTGGAGT  
GCAGAAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG  
GAGTCACCTGCAGTCTTTTGTTTTTTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA  
GTGAGGAGCCAGTAAGAAACATCTGGGTATTTGGAAACAAGTGGTCATTGTTACATTCATTT  
GCTGAACTTAACAAAACCTGTTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG  
CTTCTCAGTGCTCTCTTTCCAATATAGATGTGGTCATGTTTGACTTGTACAGAATGTTAATC  
ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA  
ATAACTTTAAACATATTCTCAAGAGAAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG  
AATACAAACAGTATACTCATG

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**FIGURE 2**

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL  
KEAALEPSMEKIFKIDQMGRWVAVAGGAAGVGLGALCYGGLGSLNEIGAIEKAVIWPQYVKDRI  
HSTYMYLAGSIGLTALSAIAISRTPVLMNFMMRGWSVTIGVTFAAMVGAGMLVRSIPYDQSP  
GPKHLAWLLHSGVMGAVVAPLTIILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL  
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGVLVLSMFLLYDTQKVIKRAEVSPMYGV  
QKYDPINSMLSIYMDTLNIFMRVATMLATGGNRKK

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**FIGURE 3**

GAAGGCTGCCTCGCTGGTCCGAATTCCGGTGGCGCCACGTCCGCCCCTCTCCGCCTTCTGCAT  
CGCGGCTTCGGCGGCTTCCACCTAGACACCTAACAGTCGCGGAGCCGGCCGCTCGTGAGGG  
GGTCGGCACGGGGAGTCGGGCGGTCTTGTCATCTTGGCTACCTGTGGGTCTGAAGATGTCGG  
ACATCGGAGACTGGTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTCGCCGCCACCGTC  
GCCGTGCCCTTGGTCGGCAAACCTCGGCCTCATCAGCCCGGCCTACCTCTTCCTCTGGCCCGA  
AGCCTTCCTTTATCGCTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG  
GTCCAGGAACCTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTCTACGCGA  
CTTGAAACAGGAGCTTTTGTATGGGAGGCCAGCAGACTATTTATTCATGCTCCTCTTTAACTG  
GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA  
TGTCAGTACTTTATGTCTGGGCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGGA  
ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG  
CTCGGTAATCAATGAGCTTATTGGAATCTGGTTGGACATCTTTATTTTTTCTTAATGTTCA  
GATACCCAATGGACTTGGGAGGAAGAAATTTTCTATCCACACCTCAGTTTTTGTACCGCTGG  
CTGCCAGTAGGAGAGGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC  
TGCTGATCAGAATGGCGGAGGCGGGAGACACAACCTGGGGCCAGGGCTTTCGACTTGGAGACC  
AGTGAAGGGGCGGCCCTCGGGCAGCCGCTCCTCTCAAGCCACATTTCTCCAGTGCTGGGTG  
CACTTAACAACCTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC  
AGTACGAGACAAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTCCACAAGTTTCACGAT  
TCTCATTTCAAGTCCTTACTGCTGTGAAGAACAATAACCAACTGTGCAAATTGCAAAACTGAC  
TACATTTTTTGGTGTCTTCTCTTCTCCCTTTCCGTCTGAATAATGGGTTTTAGCGGGTCTCT  
AATCTGCTGGCATTGAGCTGGGGCTGGGTACCAAACCCTTCCCAAAAGGACCTTATCTCTT  
TCTTGACACATGCCTCTCTCCACTTTTCCCAACCCCCACATTTGCAACTAGAAAAAGTTG  
CCCATAAAATTGCTCTGCCCTTGACAGGTTCTGTTATTTATTGACTTTTGGCAAGGCTGGTC  
ACAACAATCATATTCACGTTATTTTCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG  
AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGGAAATGCTTCGACTGACATCCGTTGTT  
AACCGTTTGGCACTCTTCAGATATTTTTTATAAAAAAGTACCACTGAGTTCATGAGGGCCA  
CAGATTGTTTATTAATGAGATACGAGGGTGGTGGTCTGGGTGTTTGTTCCTGAGCTAAGTGA  
TCAAGACTGTAGTGGAGTTGCAGCTAACATAGGGTTAGGTTTAAACCATGGGGGATGACGCC  
TTTGGCTTTTATATGTAGCCCTACTGGCTTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT  
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCCTGGGCATTG  
ATTCCCATTTCATCTCATTCTGGATATGTGTTTATTGAGTAAAGGAGGAGAGACCCTCATA  
CGCTATTTAAATGTCACTTTTTTGCCTATCCCCGTTTTTGGTTCATGTTTCAATTAATTGT  
GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA  
AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAAGGTGTGTTA  
TTTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTT  
TCGTAGGTGGGCTTTTCTATCAGAGCTTGGCTCATAACCAATAAAGTTTTTTGAAGGCCA  
TGGCTTTTACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT  
ATTGAGTGGCTGTACACTTTGAGGCAACTAAAAAGGCTTCAAACGTTTTGATCAGTTTCTT  
TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTCCCCACTCTTAAACAGTGTGAT  
GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACCTTCTCATTTTGAATAGAGTTTGTGTG  
TACTTCTCATATTTAATTTATATGATAAAATAGGTGGGGAGAGTCTGAACCTTAAGTGTCA  
TGTTTTGTTGTTTCTCTGTGGCCACAATAAAGTTTACTTGTAAAATTTTAGAGGCCATTACT  
CCAATTATGTTGCACGTACACTCATTGTACAGGCGTGGAGACTCATTGTATGTATAAGAATA  
TTTCTGACAGTGAGTGACCCGGAGTCTCTGGTGTACCTCTTACCAGTCAGCTGCCTGCGAG  
CAGTCATTTTTTCTTAAAGGTTTACAAGTATTTAGAAGTTTTCAGTTCAGGGCAAAATGTTT  
ATGAAGTTATTCCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT  
ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA  
TGACAGTGGATTCTCTTTACAAATGAAAAAATAATCCTTATTTTGTATAAAGGACTTCCC  
TTTTTGTAATAATCCTTTTTTATTGGTAAAAATTGTAAATTAAATGTGCAACTTG

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**FIGURE 4**

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFLWPEAFLYRFQIWRPITATFYF  
PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP  
LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIIGGSVINELIGNLVGHLYFFL  
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRL  
GDQ

**Transmembrane domain:**

amino acids 98-116, 152-172

**N-myristoylation site.**

amino acids 89-95, 168-174, 176-182, 215-221, 221-227, 237-243

**Glycosaminoglycan attachment site.**

amino acids 218-222

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**FIGURE 5**

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTTGCCATAGCGACCATTTTGCATTA ACTGGTTG  
GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT  
CCTTGTGGCCCAAAGGCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC  
CCTTTGGGGCGGGATGGCTGCGGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG  
CGGGGTTCTGCGAGGCCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT  
GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT  
GGCCTGTGTTCCCCTTGTTTTTGTATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTC  
ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT  
AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC  
CATTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA  
AAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTACCT  
GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT  
GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA  
AACAGTTATCAGAGGCTAAAACAGAAGAGCCCACAGTGCAATTCCAGTGAAGCTGCAATAATG  
AATAATTCCCAAGGGGATGGTGAACATTTTGCACACCCACCCTCAGAAGTTAAAATGCATTT  
TGCTAATCAGTCAATAGAACCTTTGGGAAGAAAAGTGGAAGGTCTGAACTTCCTCCCTCC  
CACAAAAGGCCTGAAGATTCCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC  
TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA  
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG  
GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG  
CAAACATTACTAAAGAGGAGATTGCTTGACAGAGAACTCAAAGAAGAAGTTATTAATAAGTA  
ATAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTC  
CTTACACTG

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**FIGURE 6**

MAAEEEEDEVEWVVESIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP  
LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEACTSPLAKTHTSQAILQP  
VLAAEDFTIFKAMMVQKNIEMQLQAIRIIQERNGVLPDCLTDGSDVVSLEHEEMKILREVL  
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS  
IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLMS  
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEKQTLLKRLLAEKLKEEVINK

**N-glycosylation sites.**

amino acids 224-228, 246-250, 285-289

**N-myristoylation site.**

amino acids 273-279

**Amidation site.**

amino acids 252-256

**Cytosolic fatty-acid binding proteins.**

amino acids 78-108

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**FIGURE 7**

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT  
TCATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA  
TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG  
GCCATTTTGGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC  
AGAAAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTA  
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT  
CCTGAGGGAAGTTCTTAGAAAAATCAAAGAGGAATATGACCAGGAA



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**FIGURE 8**

GCGTGGTTTTTGTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTG  
TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG  
TCTCAGCTCTAGGATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAACAAAC  
AGTGGAAATGGAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCACAAATGTATAC  
ATTCTTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT  
CTGCCAATGAAGAAAACAAGTATGATTATCTTCCAACCTACTGTGAATGTGTGCTCAGAACTG  
GTGAAGCTAGTTTTCTGTGTGCTTGTGTCAATTCTGTGTTATAAAGAAAGATCATCAAAGTAG  
AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTCATGAAGTGGTCCATTCTGCCT  
TTCTTTATTTTCTGGATAACTTGATTGTCTTCTATGTCCTGTCTATCTTCAACCAGCCATG  
GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAA  
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCT  
TGACTGCCGGGACTAAAACCTTACAGCACAACTTGGCAGGACGTGGATTTTCATCACGATGCC  
TTTTTCAGCCCTTCCAATTCCTGCCTTCTTTTCAGAAAGTGAGTGTCCCAGAAAAGACAATTG  
TACAGCAAAGGAATGGACTTTTCCTGAAGCTAAATGGAACACCACAGCCAGAGTTTTTCAGTC  
ACATCCGTCTTGGCATGGGCCATGTTCTTATTATAGTCCAGTGTTTTATTTCTTCAATGGCT  
AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA  
GAACAGCAAACCTCTATTTCTTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA  
GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTTATGGCCACAGTGCATTTTCAGTAGCC  
CTTATTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA  
CATGTTCCATGTCTTGATGGCCAGGTTACCACTGTCATTATCACAAACAGTGTCTGTCTCTGG  
TCTTTGACTTCAGGCCCTCCCTGGAATTTTTCTTGGAAAGCCCCATCAGTCCTTCTCTCTATA  
TTTATTTATAATGCCAGCAAGCCTCAAGTTCGGAATACGCACCTAGGCAAGAAAGGATCCG  
AGATCTAAGTGGCAATCTTTGGGAGCGTTCAGTGGGGATGGAGAAGAACTAGAAAGACTTA  
CCAAACCCAAGAGTGATGAGTCAGATGAAGATACTTTCTAACTGGTACCCACATAGTTTTGCA  
GCTCTCTTGAACCTTATTTTTACATTTTTCAGTGTTTTGTAATATTTATCTTTTCACTTTGATA  
AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAATGGTT  
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA  
ATATGAAGAATTCATTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT  
TTTCCTTGGCCTTCAAGCTTCCAAAAAAGCTTGTAAATATCATGTTAGCTATAGCTTGTATAT  
ACACATAGAGATCAATTTGCCAAATATTACAAATCATGTAGTTCTAGTTTACATGCCAAAGT  
CTTCCCTTTTTAACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT  
CATTTTGCAAGTAAAGAGCAACGGGACCCTTCTAAAAACGTTGGTTGAAGGACCTAAATAC  
CTGGCCATACCATAGATTTGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT  
TTCTCAGACACAACATCTCAGAATTTTAATTTTAGAAATTCATGGGAAATTGGATTTTTGT  
AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACCACTTGTATTTTA  
AGTCATTTAAACAAGCCACGGTGGGGCTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT  
GTCATTACTCCTGAATTATTACATTTTGGAGAATAAGAGGGCATTTTATTTTATTAGTTACT  
AATTCAAGCTGTGACTATTGTATATCTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAAC  
CAGATTGTGCTAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTCAAAGGATCACTT  
AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC  
AGTAATATATAAGTCACTTTACAGTGCTACTTCACACTTAAAGTGCATGGTATTTTTTCATG  
GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA  
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG  
CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT  
CATTTCTCAGAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA  
AGGTAATATACTATTATATAATTCAATTTGTGATATCCACAATAATATGACTGGCAAGAATTG  
GTGGAATTTGTAATTAAATAATTATTAAACCT

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**FIGURE 9**

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK  
LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAV  
IFSNFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLARGGFHHDAFF  
SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI  
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSASFVALI  
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI  
YNASKPQVPEYAPRQERIRDLSGNLWERSSSGDGEELERLTKPKSDESEDTF

**Transmembrane domains:**

amino acids 16-36 (type II), 50-74, 147-168, 229-250, 271-293,  
298-318, 328-368

**N-glycosylation sites.**

amino acids 128-132, 204-208, 218-222, 374-378

**Glycosaminoglycan attachment site.**

amino acids 402-406

**N-myristoylation sites.**

amino acids 257-263, 275-281, 280-286, 284-290, 317-323

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**FIGURE 10**

CGTGCCTGCGCAATGGGTGTGCGGTCCGCTTTTTCCCAATCCGGACGTAATCGTGGTTTTTG  
TTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTGTAGCTTCTCCAC  
GTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTCAGCTCTAG  
GATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAAAAACAGTGGAAATGGAA  
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATACATTCCTGCTAGG  
TGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATTCTGCCAATGAAG  
AAAACAAGTATGATTATCTTCCAATACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT  
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAAGAAAGATCATCAAAGTAGAAATTTGAAATA  
TGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCTGCCTTTCTTTATTTCC  
TGGATAACTTGATTGTCTTCTATGTCCTGTCTATCTTCAACCAGCCATGGCTGTTATCTTC  
TCAAATTTTAGCATTATAACAACAGCTCTTCTATTCAGGATAGTGCTGAAGAGGCGTCTAAA  
CTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCTTGACTGCCGGGA  
CTAAACTTTA

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**FIGURE 11**

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGCCGGCTTGGCTAGCGCGCGGGCGGCC  
GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT  
CCCGTCTACCAGGTCCCAAGCGGCGTGCCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG  
AGCGGCTCCGCGGCGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCCGGCCCA  
GGTGAAGAAAGAACCGAAAAAGAAGAAACAACAGTTGTCTGTTTGCAACAAGCTTTGCTATG  
CACTTGGGGGAGCCCCCTACCAGGTGACGGGCTGTGCCCTGGGTTTCTTCCTTCAGATCTAC  
CTATTGGATGTTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC  
CTGGGATGCCATCACAGACCCCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC  
TGGGTGCGCTTATGCCCTGGATCATCTTCTCCACGCCCCCTGGCCGTCATTGCCTACTTCCTC  
ATCTGGTTTCGTGCCCCACTTCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT  
CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTTCATCAGCA  
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC  
AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG  
ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATAACATGGCACCACCTTCACAC  
AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTG  
TGCTGTATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCAGCAGTCTG  
AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATAATCAAACTT  
ATTACTGGCTTCTCTTACCTCCTTGGCTTTTCATGCTGGTGGAGGGGAACCTTGTCTTGT  
TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT  
CGGCCACTTTAACCATTCCCCTCTGGCAGTGTTTCTTGACCCGGTTTGGCAAGAAGACAGCT  
GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA  
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC  
TACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT  
GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTACCAAGTTTGCCTCTGGAGTGTC  
ACTGGGCATTTCTACCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC  
CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG  
CTGGGCCTGCTGCTCTTCAAAATGTACCCCATTGATGAGGAGAGGCGGCGGCAGAATAAGAA  
GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG  
AGCTGGCTAGCATCCTCTAGGGGCCGCCACGTTGCCCCGAAGCCACCATGCAGAAGGCCACAG  
AAGGGATCAGGACCTGTCTGCCGGCTTGTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA  
CTGAAGACTCAAGGAGGTGGCCAGGACACTTGTGTGCTCACTGTGGGGCCGGCTGCTCTG  
TGGCCTCCTGCCTCCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA  
TGCCAAGGACTGATCGGGCCTAGCCCGGAACATAATGTAGAAACCTTTTTTTTACAGAGCC  
TAATTAATAACTTAATGACTGTGTACATAGCAATGTGTGTGTATGTATATGTCTGTGAGCTA  
TTAATGTTATTATTTTCATAAAAGCTGGAAAGC

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**FIGURE 12**

MWLRWALSLPPSSCLWAEFGMPSTPWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG  
SCPTSHTARPIGTCFSTIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL  
GTAIQQQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV  
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPIYIKLITGFLFTSLAFMLVEGNFVLFCT  
YTLGFRNEFQNLALLAIMLSATLTPIWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI  
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG  
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKAL  
QALRDEASSSGCSETDSTELASIL

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**FIGURE 13**

GGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT  
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTGA  
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACCTTA  
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTTT  
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC  
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG  
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAAC  
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT  
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG  
GAACCGAGCCCAT

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**FIGURE 14**

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT  
ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAACAGAAAACCTGTTAGAAATGT  
GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT  
TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT  
CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG  
CAGTTTTATGCATTGCTACCATTTATGTTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA  
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTAAGTGGAACTGAGTTGTTTAGG  
ACTTTCTATTGTGGCAAAACTTCCAGAAAACAACCCTTTTGTCTGCACATGTAAGTGGAGCTG  
TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCCTACCAAATG  
CAGCCCCAAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG  
AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG  
ATTTAGAACAGAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT  
ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCCTTTGGTTTTTTCCTGACTTACATTCGTGA  
TTTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCTCTATGACACTG  
CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCAGAGATATTTTGATGAAAGGAT  
AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTACAGAAGTTGCTTA  
TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA  
ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA  
TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAGACTATG

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**FIGURE 15**

MWWFQQGLSFLPSALVIWTSAAFIFSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI  
AAVLCIATIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG  
AVLTFMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG  
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYYIRDFQKISLRVEANLHGLTYD  
TAPCPINNERTRLLSRDI



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**FIGURE 16**

CGGACGCTTGGGCNGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCTGATGCCGAGT  
TCCGTCTCTCGGGTCTTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA  
GTGCTTCGCGCTTCCGGAGAAAATCAGCGGTCTAATTAATTCCTCTGGTTTGTTGAAGCAGT  
TACCAAGAATCTTCAACCCTTCCCACAAAAGCTAATTGAGTACACGTTCCCTGTTGAGTACA  
CGTTCCTGTTGATTTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTTTGTGAA  
GTTGTAAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCT  
TCAGCCCTTGTAATTTGGACATCTGCTGCTTTCATATTTTCATACATTACTGCAGTAACACT  
CCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGGTACAGTANC

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**FIGURE 17**

CCCACGCGTCCGCCCCGCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGGG  
CCGGGGTGCGGAGCCGACATGCGCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC  
CTTCGCCTTGTAATTGCTGTGACGCGACTGCCCCGCGGGCGGAGACTGGGCTCCACCGAGG  
AGGCTGGAGGCAGGTCGCTGTGGTTCCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG  
GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCTGCTCTTCTGCGGCGCCTA  
CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT  
TGTTTGGGCCATGGCTGGGGCTTCTGCTGTGCTGTGTGTTGACCTCGGTGGGTGCCACATGC  
TGCTACCTGCTCTCCAGTATTTTTGGCAAACAGTTGGTGGTGTCTACTTTTCTGATAAAGT  
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAACAGAAACAGCTTGTTTTTTTTCTTATTGTTTT  
TGAGACTTTTCCCCATGACACCAAACCTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT  
CCCATCGTGCAGTTCTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTCATCTGTGT  
GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCTGGGACACTG  
TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAAATCCTGGAACCCTCATTAAAAAATT  
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA  
CACATTGATCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA  
TGTGGTCCCTCTAAAGCCCCCTCATTTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG  
CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT  
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT  
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATTC  
ACAAGGTCAAGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAAT  
ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC  
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT  
CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

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**FIGURE 18**

MRPLLGLLLVFAGCTFALYLLSTRLPGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR  
KEHQAYVFLLFCGAYLYKQGFAIPGSSFLNVLGALFGPWLGLLLCCVLTSVGATCCYLLSS  
IFGKQLVVSYPDPKVALLQRKVEENRNSLFFFLFLRLFPMTPNWFLNLSAPILNIPVQFF  
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ  
LNETSTANHIHSRKDT

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domains:**

amino acids 101-123, 189-211

**N-glycosylation sites.**

amino acids 172-176, 250-254

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 240-244, 261-265

**N-myristoylation site.**

amino acids 13-19, 104-110, 115-121, 204-210

**Amidation site.**

amino acids 27-31

**Prokaryotic membrane lipoprotein lipid attachment site.**

amino acids 4-15

**Protein splicing proteins.**

amino acids 25-31

**Sugar transport proteins.**

amino acids 162-172

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**FIGURE 19**

CCGAGGCGGGAGGAGCCCCGAGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT  
CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA  
TAGGAAAATAACTTGGGATTTTATATTGGAAGACATGGATCTTGCTGCCAACGAGATCAGCA  
TTTATGACAACTTTCAGAGACTGTTGATTTGGTGAGACAGACCGGCCATCAGTGTGGCATG  
TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC  
CCCCCGCAGTATCCTCTCCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT  
TGCTCACTGCCTACTTTGTGATTC AACCTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTCT  
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA  
GAAGTACATGTCAGAAAATAAGGGAGTTCCTCTGCATGGGGGTGATGAAGACAGACCCTTTC  
CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTGACC  
AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA  
ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC  
AGCATTTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG  
TGGTGGCGCTGCTTTCCTGAGCGGTGGTTCCCATTTCTTATCCATGGAGGAGACCTCTGAA  
CAGATCACAAATGTTACGTGAGCTTTTTCTGTTTTCACTCACCTGCCATTTCCAAAAGATG  
CCTCTTTAAACAAGTGCTCCTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG  
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTTCCA  
GTGCCGAAGACATTGTCAGTCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTGCG  
ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT  
GGAACCGCTTTCTCAGAACTGTAGGAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA  
AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAAACGATGAAACTGCAAAAA

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**FIGURE 20**

MDLAANEISIIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY  
KVLATLGLILLTAYFVIQPFSPPLAPEPVLSGAHTWRSLIHHIRLMSLPPIAKKYMSENKGVPL  
HGGDEDRPFPDFDPWWTNDCEQNESEPIPANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT  
GKPLLEEEIQHFLCQYPEATEGFSEGGFAKWWRCFPERWFFPYWRRPLNRSQMLRELPV  
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQRRHCQSVAMP  
IEPGDIGYVDTTTHWKVYVIARGVQPLVICDGTAFSEL

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**FIGURE 21**

CCACGGTGTCCGTTCTTCGCCCCGGCGGCAGCTGTCCCCGAGGCGGGAGGAGCCCCGAGGGGCG  
CGAGCCCCGCATGAATCATTGTAGTCAATCATTTTCCAGTTCTCAGCCGTTTCAAGTTGTGATC  
AAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAATAGGAAAATAACTTGGGATTTTATATT  
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTTATGACAACTTTCAGAGACTGTTG  
ATTTGGTGAGACAGACCGGCCATCAGTGTGGCATGTCAGAGAAGGCAATTGAAAAATTTATC  
AGACAGCTGCTGGAAAAGAATGAACCTCAGAGACCCCCCGCAGTATCCTCTCCTTATAGT  
TGTGTATAAGGTTCTCGCAACCTTGGGATTAATCTTGCTCACTGCCTACTTTGTGATTCAAC  
CTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTGTGGAGCTCAC

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**FIGURE 22**

CCCACGCGTCCGCCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG  
CAGGGTCCCCACTTGCAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG  
CCACTGGTGCACGCTGCTAGACCGTGCCTATGAGCCGCTGGGGCTGCAGTGGGGACTGCC  
CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA  
CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACCATGTCCAGTTTCGAAATG  
GACACGTATGCTAAGAGCCACGACCTTATGTAGGTTTCTGGAATGCCTGCTATGACATGCT  
TATGAGCAGTGGGCAGCGGCCAGTGGGAGCGGCCAGAGTCGTGCGGCCCTTCCAGGAGC  
TGGTGTGGAACCTGCGCAGAGGCGGGCGGCCTGGAGGGGCTACGCTACACGGCAGTGCTG  
AAGCAGCAGGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGCGCTGTGGCGCCAGCT  
CGCCAGCCCATGTGGGGCCTGGGCGCTGAGGGACACTCCCATCCCCCGCTGGAACTGTCCA  
GCGCCGAGACATATTCACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCCTCAC  
CTGGAAGCCAGCGCTCTCCGAGACAATCTGGGTGAGGTTCCTTGACACCCACCGAGGAGGC  
CTCACTGCCTCTGGCAGTGACCAAGAGGGCCAAAGTGAGCACCCACCCGAGTTGCTGCAGG  
AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCCGATGGAGGCAGCAGAACTG  
GATGAGCAGCGTGAGAAGCTGGTGTGTCGGCCGAGTGCCAGCTGGTGACGGTAGTGGCCGT  
GGTCCCAGGGCTGCTGGAGGTCAACACAGAATGTATACTTCTACGATGGCAGCACTGAGC  
GCGTGGAACCCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCCACTGCGTGAG  
GTCCACCTGCGGCGTTTCAACCTGCGCCGTTTACGCACTTGAGCTCTTCTTTATCGATCAGGC  
CAACTACTTCTCAACTTCCCATGCAAGGTGGGCACGACCCAGTCTCATCTCCTAGCCAGA  
CTCCGAGACCCAGCCTGGCCCCATCCCAACCCATACCCAGGTACGGAACCAAGGTGTACTCG  
TGGCTCCTGCGCCTACGGCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT  
GCTGCGTGCCCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACCTCGAGTACT  
TGATGCAACTCAACACCATTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTC  
CCCTGGGTCTGCAAGGACTACGTGTCCCAACCCCTGGACCTCAGCAACCCAGCCGTCTTCCG  
GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCCAGCTCGTGAGGGAGAAGT  
ATGAAGCTTTGAGGACCCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCTACTCTC  
AATGACAGCAGGCGTGATGCACTACCTCATCCGCGTGAGGCCCTTCACCTCCCTGCACGTCCA  
GCTGCAAAAGTGGCCGCTTTGACTGCTCCGACCGGCAGTTCCACTCGGTGGCGGCAGCCTGGC  
AGGCACGCCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGAATTCTTCTACTTTCT  
GACTTCTTGAGAAACAGAACCGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT  
AGGCGATGTGGTGCTACCCCGTGGGCCAGCTCTCTGAGGACTTCATCCAGCAGCACCGCC  
AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCTTTGGC  
TACAAGCAGCGGGGGCCAGCCGCCGAGGAGGCCCTCAATGTCTTCTATTACTGCACCTATGA  
GGGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATTA  
TCAGCAACTTTGGGCAGACTCCCTGTGAGCTGCTGAAGGAGCCACATCCAACCTCGGCTCTCA  
GCTGAGGAAGCAGCCCATCGCCTTGACCGCTGGACACTAATCACTACCTAGCATCTTCCAGCA  
CCTGGACGAACCTCAAGGCATTCTTCGACAGAGGTGACTGTGAGTGCCAGTGGGCTGTGGGCA  
CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAGACCCC  
ACCATGGGCAGCCACAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT  
GAGTGGACAAGCACTGGCAGTGGCCCCGGATGGAAAGCTGCTATTACGCGGTGGCCACTGGG  
ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTGCCAC  
CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCC  
GGACACCAGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTGAGTAGGCCTGGCAC  
CAAAGCCTGTGCAAGTCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT  
GAACTTGACATGGCTGTGTCTGGATCTGAGGATGGAAGTGTGATCATACACACTGTACGCCG  
CGGACAGTTTGTAGCGGCACTACGGCCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC  
TGGCATTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCTTGGGGCC  
CAGGTACCTACTCCTTGACCTGTATTAGTCAATGGGAAGTTGCGGGCTTCACTGCCCCCT  
GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCAGT  
GCGCCCTGCACATCTCCAACATAACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG  
GTGGCTTCCGAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCTGGAGGA  
TGGCAAGCTCATCGTGGTGGTTCGCGGGGCGCCCTCTGAGGTGCGCAGCAGCCAGTTCGCGC  
GGAAGCTGTGGCGGTCTCGCGGCGCATCTCCAGGTGTCTCGGGAGAGACGGAATACAAC  
CCTACTGAGGCGCGCTGAACCTGGCCAGTCCGGCTGCTCGGGCCCCGCCCCGGCAGGCCTG  
GCCCCGGGAGGCCCGCCAGAAGTCGGCGGGAACACCCCGGGGTGGGCAGCCAGGGGGTGA  
GCGGGGCCCCACCTGCCAGCTCAGGGATTGGCGGGCGATGTTACCCCTCAGGGATTGGCG  
GGCGGAAGTCCCGCCCCCTCGCCGGCTGAGGGGCGCCCTGAGGGCCAGCACTGGCGTCT

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**FIGURE 23**

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL  
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN  
HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELALELETP  
MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETEEGIGYDFRRP  
LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV  
RNQVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRTYNDL  
SQYPVFPWVLQDYVSPTLDLSNPAVFRDLSKPIGVVNPKHAQLVREKYESFEDPAGTIDKFH  
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDSCDRQFHSVAAAWQARLESPADVKEIP  
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPPWASSPEDFIQQHRQALESEYVSAHLHEW  
IDLIFGYKQRGPAEEALNVFYCYTYEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP  
HPTRLSAEEAAHRLARLDTNSPSIFQHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF  
SFSKDPTMGSHKTQRLLSGPWPVPGSGVSGQALAVAPDGKLLFSGGHWGDSLRTALPRGKLL  
SQLSCHLDVVTCLALDTCGIYILISGSRDTTCMVWRLHQQGLSVGLAPKPVQVLYGHGAAS  
CVAISTELDMAVSGSEDGTVIIHTVRRGQFVAALRPLGATFPGPFIHLALGSEGQIVVQSSA  
WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVTEDFVLLGTAQCALHILQLNTLLPAA  
PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVAGQPSEVRSSQFARKLWRSSRRISQVSS  
GETEYNPTPEAR

**N-glycosylation site.**

amino acids 677-681

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 985-989

**Tyrosine kinase phosphorylation site.**

amino acids 56-65, 367-376, 543-551

**N-myristoylation site.**amino acids 61-67, 436-442, 604-610, 610-616, 664-670, 691-697,  
706-712, 711-717, 769-775, 785-791, 802-808, 820-826, 834-840,  
873-879, 912-918, 954-960



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**FIGURE 24**

CGGACGCGTGGGCGGACGCGTGGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCC  
CACGGCCACCTTGTGAACTCCTCGTGCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT  
CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGGGCTCTTC  
TGGACCCTTAAGTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT  
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC  
GCACACTCCGTTACCACACTGGGTCAATTGGCATTGAGAGCCCTCATCCTGACCCTTGTGCAG  
ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGC  
CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC  
TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA  
AATGCGTTCATGCTACTCATGCGAAACATTTGTGAGGGTGGTCTGCTGGACAAAGTCACAGA  
CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTCTGGAGGCGTGGGGGTCTGTCTTCTTTT  
TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCCACCTCAACTATTAC  
TGGCTGCCCATCATGACCTCCATCCTGGGGGCCTATGTCATCGCCAGCGGCTTCTTCAGCGT  
TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG  
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC  
GAGGCGCCCCCGGACAACAAGAAGAGGAAGAAGTGAAGCTCCGGCCCTGATCCAGGACTGC  
ACCCACCCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT  
AAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG  
AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC  
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTATCCAGCTAC  
TCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA  
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAAACAA  
AAAGATTTTATTAAAGATATTTTGTAACTC

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**FIGURE 25**

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVGLGF  
WTLNWWLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQ  
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK  
NAFMLLMRNIVRVVLDKVTDLLFFGKLLVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY  
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYSKSLKILGKKN  
EAPPDNKKRKK

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**FIGURE 26**

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT  
GGCTATGTTTCGTGTCCGATTTCGCGAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC  
TTCTCTTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTT  
CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC  
ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAAACTGTGGAGCTAATGTAG  
ACCTATTGGATATTCTTCAACCTGATGAAGACACTATATTCTTTGTGTGTGACTCCCATAGG  
CCAGTCAATGTGTCGTCATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA  
TGACCTTGAAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT  
CAGGAAATGACAGTGATGGGTGAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA  
GTGGAGCAAACCATGCGGAGGAGGCAGCGGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT  
CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG  
CTTGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC  
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCCTGCAGCG  
CCACGTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA  
CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC  
AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA  
GCGGCTCCAGGAGTTCCTTGACAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC  
AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA  
TTTGGGATGAAGGACATGCGCGTGACAGCTTTCAGCATTCAATTTGGGTTCAAGCACAAAGTT  
TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT  
CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG  
TACCATGGCCTGGAACCTGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC  
CTTTGCACCAACCTCGTCATCTCCCAGGGGCCTTTCTGTACTGCTCTCTCATGGAGGGCAC  
TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA  
AGTCCTTTGTGTGTTTCGACAAAGAACCGGCGCTGCAAACCTGCTGCCCCCTGGTGATGGCTGCC  
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCAGAGACCGACAGCTC  
GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA  
TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT  
CTGGACGCACTTATTTCCCTCCTGTCCTAGGAAATTTGATTCTTCCAGAATGACCTTCTTATT  
TATGTAACGGCTTTTCAATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT  
TTTTATTAAATAAAATGCTTATTTTAGGAAA

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**FIGURE 27**

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETA  
LEHKEQFHYFILINCGANVDLLDILQPDEDITIFFVCDSHRPVNVNVYNDTQIKLLIKQDDD  
LEVPAIEDIFRDEEEDDEHSGNDSGSEPSEKTRLEEEIVEQTMRRRQRREWEARRRDILF  
DYEQYEHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLRH  
VSRHNRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSLCNTSYTAARFKLWSVHGQKR  
LQEF LADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTF SIHFGFKHKFL  
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLRSNLDKLYHGLELAKKQLRATQQTIASCL  
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP  
LSMEHGTVTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNFDSLVIELKAEDRSKFL  
DALISLLS

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**FIGURE 28**

GTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGTGGCTATGNTCGTGTCCGATTTCCGCA  
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCCTTCTCTTCGTGGCCTCGGANGTGGAT  
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGACCANGTGCAATATANGCT  
GGTTCCAGTTTCTGGGTGGCAAGAACTTGAACTGCATTTCTTGAGCATAAAGAACAGTTTC  
ATTATTTTATTCTCATAAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT  
GAAGACACTATATTCTTTGTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA  
CGATACCC

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**FIGURE 29**

CAGGAACCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC  
CACGAAGGGACGATACCAGAAAAACACCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG  
GCTGACTTTGGCTATAGAAAAAAGAAAGGAACGAAAAGAGACAGTTTTTTTTTGGAAAGCTAA  
GTCTTCCCTTTATCGAGTCAAGAAACCCCCCTTCTTGAGCTATTTACAGCTTTTAACAATT  
GAGTAAAGTACGCTCCGGTCACCA**ATGGT**GACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC  
CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC  
CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCTGGATCCTGCCCATGTATCCTCAG  
CCTCTTCTCCTCCGGCCGCCCCACGCCCTGCCTGAGATCAGACCCTACATTAATATCACCATC  
CTGAAGGGTGACAAAGGGGACCCAGGCCCAATGGGCCTGCCAGGGTACATGGGCAGGGAGGG  
TCCCCAAGGGGAGCCTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGGAGATGGGCAGCCCCG  
GCGCCCCGTGCCAGAAGCGCTTCTTCGCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC  
GGCGAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA  
CATGGCGACCGGCCAGTTTGCTGCTCCCTGCGTGGCATCTACTTCTTCAGCCTCAATGTGC  
ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTCATC  
CTGTACGCGCAGCCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC  
CTACGGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCGAGAAGCCATCTACAGCA  
ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGAC**TGAGG**  
CCTCTGGGCCACCCCTGCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTGCAGGGCTCAG  
TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCCGGGGACCTGGCATTCTGGGGAGA  
CCCTGCTTCTATCTTGCTGCCATCATCCCTCCCAGCCTATTTCTGCTCCTCTCTCTCTCT  
TGGACCTATTTTAAAGAGCTTGCTAACCTAAATATTCTAGAACTTTCCCAGCCTCGTAGCCC  
AGCACTTCTCAAACCTTGAAATGCATGCGAATCACCCGGGGTTCGTGTTAAATGCAGATTCT  
GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCTGGGTGATGCTG  
ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG  
TACTTTCTGAACATTCTGGAATCCTCCCCACATTCTAGAACTTCTCCCAACATTTTTTTTTCT  
TGAGACAGAGTCTTGCTCTGTTGCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCACTGC  
AACCTCTGCCCTCCCGGGTTCAAGCGATTCTCTGCTCAGCCTCCCTAGTGGCTGGGATTAC  
AGGCGCCTGCTACCATGCCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTACCATA  
TTGGCCAGGCTGGTCTTGAACCTCCTGACTTCAGGTGACCCACCCGCTCGGCCTCTCAAAAT  
GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT  
CCCTCCAGGGCTCCCCGTGCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC  
TGCACCACTGCAGCCACCGTTCAATTTATTCATTCAATTAACACTGAGCACTCACTCTGTGCT  
GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGACTGGCCA  
GTCCAGCCCAGGCGGGGAGAGATGTGTACATAGGTTTTTAAAGCAGACCCAGAGCTCATGGGG  
GCCTGTGTTCTGGGTGTTTCAAGTGCTGCTGGTCCCTCCATTACCCACTGCTCCCCAAGGCTGG  
TGGGACGGGGTCCCGGTGGCAGGGGCAGGTATCTCCTTCCCGTTCTCATCCACCTGCCCAG  
TGCTCATCGTTACAGCAAACCCAGGGGGCCTTGGCCAGGTCAAGGGTTCTGTGAGGAGAGG  
ACCCAGGAGTGTGGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA  
TAGCTCTCCCCACAGCTGATACGGCATCCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC  
CTTCCTGCCTCCTCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT  
GAACTTCCGTTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGTCCCCAGGTGCT  
CTCTGCCCCCTCATGCCCCCTCTCACCGGCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG  
CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGCTGCCTTTAC  
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG  
AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTTCTTCTTCCAGGGTGGGGTGGCCTGGT  
GTTCCCTAGCCTTCCAACCCAGGTGGCCTGCCCTTCTCCCCAGAGGGAGGCGGCCTCCG  
CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCGGGGGGTGATCTCTGGTGCTCAC  
AGCCGAGGGAGCCGTGGCTCCATGGCCAGATGACGGAAACAGGGTCTGACCAAGTGCCAGGA  
AGACCTGTGCTATAAACCACCTGCCTGATCCTGCCCTGCCTGACCCCGCCACGCCCTGCC  
GTCCAGCATGATTAAAGATGCTGTCTCCTCTTGAAAAA

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**FIGURE 30**

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSSGRPH  
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPPGQSGDKGEMGSPGAPCQKRF  
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET  
YVHIMHNQKEAVILYAQPSEERSIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT  
FSGHLIKAEDD

**Important features:****Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 72-75

**Clq domain proteins.**

amino acids 144-178, 78-111 and 84-117

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**FIGURE 31**

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCCGACCCGCCAGGAAAGACTG  
AGGCCGCGGCCTGCCCCGCCCCGGCTCCCTGCGCCGCGCCGCTCCCCGGGACAGAAGATGTG  
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCTGGGGTGCAGG  
GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCCGCCAGGGG  
ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT  
CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGCTCCTGGACCTGTCAC  
AGAACCAGATCGCCAGCCTGCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG  
GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT  
CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC  
TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCCGCTGCGC  
CTGCCCCGCCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCCGGCAT  
CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACG  
AGGGGCTCTTACGCCGCTTGCGCAACCTCCACGACCTGGATGTGTCCGACAACAGCTGGAG  
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACAC  
CCGCATTGCCCAGCTGCGGCCCCGAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATG  
TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG  
CTGCTGGCAGCTGCCCCGAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCCTG  
GGTGC GCGAGAGCCACGTCACTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCGCCCA  
AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCCAGCCACCACC  
ACCACAGCCACAGTGCCCAACCACGAGGCCCGTGGTGC GGGAGCCCCACAGCCTTGTCTTCTAG  
CTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGGCCACTGAGGCCCCCAGCCCGCCCTCCA  
CTGCCCCACCGACTGTAGGGCCTGTCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTC  
AATGGGGGCACATGCCACCTGGGGACACGGCACCACTGGCGTGCTTGTGCCCCGAAGGCTT  
CACGGGCCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCCAGCCCTACACCAGTCA  
CGCCGAGGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTGCGC  
GTGGGGCTGCAGCGCTACCTCCAGGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTA  
TCGCAACCTATCGGGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTG  
AGTACACGGTCACCCAGCTGCGGCCCAACGCCACTTACTCCGTCTGTGTATGCCTTTGGGG  
CCCGGGCGGGTGCCGGAGGGCGAGGAGGCCTGCGGGGAGGGCCATACACCCCCAGCCGTCCA  
CTCCAACCACGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTTGCGCCCCG  
CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGACGCTACTGTGTGCGGCGG  
GGGCGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCCCT  
GGAAGTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG  
AGGCCCTGCCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCAGGGCCTGGCCTC  
CAGTCACCCCTCCACGCAAAGCCCTACATCTAAGCCAGAGAGAGACAGGGCAGCTGGGGCCG  
GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC  
CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA  
CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCAGCTGACGAGCCCTAACGTCCCCAGAAC  
CGAGTGCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG  
GGCCCTGCCATGTGCTGGTAACGCATGCCTGGGTCTGCTGGGCTCTCCCACTCCAGGCGGA  
CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG  
TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAGAACTGGAAAGGAAGATGCTTTA  
GGAACATGTTTTGCTTTTTTAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG  
GGAAGATGTTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTGTAAAGACAAACGATGATATG  
AAGGCCTTTTGTAAAGAAAAATAAAAGATGAAGTGTGAAA



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**FIGURE 32**

MCSRVP LLLPL LLLL LALGPGVQGCPSGCQCSQPQT V FCTARQGT TVPRDVPPDTVGLYVFEN  
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR  
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNSLLALEP  
GILDTANVEALRLAGLGLQQLDEGLFSRLRNLDLDVSDNQLERVPPVIRGLRGLTRLRLAG  
NTRIAQLRPEDLAGL AALQELDVSNLSLQALPGDLSGLFPRLRLLAAARNPFNCVCPLSWFG  
PWVRESHVTLASPEETRCHFPKNAGRLLLELDYADFGCPATTTTATVPTRPVVREPTALS  
SSLAPTWLSPTAPATEAPSPSTAPPTVGPVPQPDQCPPSTCLNGGTCHLGTRHHLACLCPE  
GFTGLYCESQMGQGRPSPTPVT PRPPRS LTLGIEPVSP TSLRVGLQRYLQGS SVQLRSLRL  
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA  
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPAG  
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGPGLQSPLHAKPYI

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**FIGURE 33**

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGCAAGCCGTGGGGGTTTTGAGCTCAT  
CTTCATCATTTCATATGAGGAAATAAGTGGTAAATCCTTGGAATACAATGAGACTCATCAG  
AAACATTTACATATTTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG  
AAGAAAGGGAAGTATGACCAACTGCTCCAAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG  
ACCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTTCA  
TTTTCATTTCTGTCTCCAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG  
ATCTCAAACCTTTGAATTCACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG  
AAGAGTGTAACTTGGTATTTACTGGCAGGTCTCAGGTATTTAGATCTTTCTTTAATGACTT  
TGACACCATGCCTATCTGTGAGGAAGCTGGCAACATGTCACACCTGGAAATCCTAGGTTTGA  
GTGGGGCAAAAATACAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC  
TTCTTAGGATTTCAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCATCTTAAACACAAC  
AAAACCTGCACATTTGTTTTACCAATGGACACAAATTTCTGGGTTCTTTTGCCTGATGAATCA  
AGACTTCAAAAATATTAGAAATGACAAATATAGATGGCAAAGCCAAATTTGTAAGTTATGAA  
ATGCAACGAAATCTTAGTTTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA  
TTTACTCTGGGACGACCTTTTCCTTATCTTACAATTTGTTTGGCATACATCAGTGGAACT  
TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCATTTGACTAC  
TCAAATACTGTAATGAGAACTATAAAATTTGGAGCATGTACATTTTCAGAGTGTTTTACATTC  
ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG  
CACAAATGCCACACATGCTTTTCCCGAATTATCCTACGAAATTCGAATATTTAAATTTTGCC  
AATAATATCTTAACAGACGAGTTGTTTTAAAGAAGTATCCAAGTGCCTCACTTGAAAACCT  
CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC  
CCTTGGAACTCTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAATTTGCTCA  
TGGCCAGAACTGTGGTCAATATGAATCTGTCATACAATAAATTGCTGATTCTGTCTTCAG  
GTGCTTGCCCAAAGTATTCAAATACTTGACCTAAATAATAACCAATCCAACTGTACCTA  
AAGAGACTATTCATCTGATGGCCTTACGAGAACTAAATATTGCATTTAATTTTCTAACTGAT  
CTCCCTGGATGCAGTCATTTTCAGTAGACTTTTCAGTTCTGAACATTGAAATGAACCTTCATTCT  
CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAACTCTAAATGCGGGAAGAA  
ATCCATTCCGGTGTACCTGTGAATTAATAAATTTTCATTTCAGCTTGAAACATATTCAGAGGTC  
ATGATGGTTGGATGGTCAGATTCATACACCTGTGAATACCCTTTAAACCTAAGGGGAAGTAG  
GTTAAAGACGTTTCATCTCCACGAATTATCTTGCAACACAGCTCTGTTGATTGTCACCATTG  
TGGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC  
TGGTATCTCAGGATGCTAGGTCATGTCACACAAACATGGCACAGGGTTAGGAAAACAACCCA  
AGAACAACCTCAAGAGAAATGTCCGATTCCACGCATTTATTTTCATACAGTGAACATGATTCTC  
TGTGGGTGAAGAATGAATTGATCCCCAATCTAGAGAAGGAAGATGTTTCTATCTTGATTTGC  
CTTTATGAAAGCTACTTTTGACCCCTGGCAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA  
GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCACTTTGTCCAGAAATGAGTGGTGCCATT  
ATGAATCTACTTTTGCCCAACCAATCTCTTCCATGAAAATTTCTGATCATATAATCTTTATC  
TTACTGGAACCCATTCCATTCTATTGCATTCCCACCAGGTATCATAAACTGAAAGCTCTCCT  
GGAAAAAAGCATACTTGGAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA  
ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA  
TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT  
ATAAAATCCACAGTCTTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA  
CAACCTTTATGATGGCAATTTGACAATATTTATTAATAAATAAATAAATGGTTATTCCCTTCATA  
TCAGTTTCTAGAAGGATTTCTAAGAATGTATCCTATAGAAACACCTTCACAAGTTTATAAGG  
GCTTATGGAAAAGGTGTTTCATCCAGGATTGTTTATAATCATGAAAATGTGGCCAGGTGC  
AGTGGCTCACTCTTGTAATCCCAGCACTATGGGAGGCCAAGGTGGGTGACCCACGAGGTCAA  
GAGATGGAGACCATCCTGGCCAACATGGTGAAACCTGTCTCTACTAAAATACAAAAATTA  
GCTGGGCGTGATGGTGCACGCCTGTAGTCCCAGCTACTGGGAGGCTGAGGCAGGAGAATCG  
CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT  
GACAGAGCGAGACTCCATCTCAAAAAAAGAAAAAAGAAAAAATGAAAAACATCC  
TCATGGCCACAAAATAAGGTCTAATTCATAAATATAGTACATTAATGTAATATAATATTA  
CATGCCACTAAAAAGAATAAGGTAGCTGATATTTCTGGTATGGAAAAACATATTAATAT  
GTTATAAACTATTAGGTTGGTGCAAACTAATTGTGGTTTTTGGCATTGAAATGGCATTGAA  
ATAAAAGTGTAAGAAATCTATACCAGATGTAGTAACAGTGGTTTTGGTCTGGGAGGTTGGA  
TTACAGGGAGCATTTGATTTCTATGTTGTGTATTTCTATAATGTTTGAATTGTTTAGAATGA  
ATCTGTATTTCTTTTATAAGTAGAAAAAATAAAGATAGTTTTTACAGCCT

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**FIGURE 34**

MRLIRNIYIFCSIVMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ  
LQSSDFHSVSKLRVLILCHNRIQQDLKTFFFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL  
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP  
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL  
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR  
VFYIQQDKIYLLLTkMDIENLTISNAQMPHMLFPNYPTKFQYLNFAANNILTDELfKRTIQLP  
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSQNLLOHKNDENCsWPETVVNMNLSYNKLS  
DSVFRCLPKSIQILDNNNQIQTVPKETIHLMALRELNIAFNFLTDLPGCsHFSRLSVLNIE  
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN  
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVGLAVAFCCCLHFDLPWYLRMLGQCTQTWHRV  
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI  
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHNNLFHENSdHIILILLEPIPFYCIPTRYHK  
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM  
RTDCL

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**FIGURE 35**

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAAACCTGCCTCCAAGGACCGGCCTCGGAGGGGTGCGCGGGAAAGG  
GAGGGAAGAAAGGAAGGGCGGGGCGCCCCCTGCGCCCGCCCGCGCCTCTGCGCGCCCTGTCCGCCCCGGC  
CCAGCCCAGCCCAGCCCCGCGGGCCGGTACACGCGCAGCCAGCCGGCCGCCTCCGCGCCCAAGCGCGCCGCT  
CTGCTGTGCCCTGCGCCCTTGGCCCGCGCCAGCTTCTGCGCCCGCAGCCCGCCGGCGCCCCGGTGACCGTGA  
CCCTGCCTTGGGCGCGGGGCGGAGCAGGCATGTCCCGCCCGGGGACCGCTACCCAGCGCTGGCCCTGGTGCTC  
CTGGCAGTGACCCTGGCCGGGGTCGGAGCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACGGGCAGGAGAT  
CTGGAGCCGGGAGCCCTACTACGCGCGCCCGGAGCCCGAGCTCGAGACCTTCTCTCCGCCGTGCTGCGGGG  
CCGGGAGGAGTGGGAGCGGCGCCGCGAGGAGCCAGGCCGCCAAGAGGGCCACCAAGCCCAAGAAAGCTCCC  
AAGAGGAGAAGTCGGCTCCGGAGCCGCCTCCACCAGGTAAACACAGCAACAAAAAGTTATGAGAACCAAGAG  
CTCTGAGAAGGCTGCCAACGATGATCACAGTGTCCGTGTGGCCGTGAAGATGTCAGAGAGAGTTGCCACCTC  
TTGGTCTGGAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCCTGGGGGCA  
CATCGAGGGAGACTCAACATCCAGGCGGGCATTAAATGAAAAATGATTTTATGACGGAGCGTGGTGCGCGGAAG  
AAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCTGACCAGATTCACTGGTGTCACTCAAGGGA  
GGAACTCCCTCTGGCTGAGTGACTGGGTGACATCCTATAAGGTGATGGTGAGCAATGACAGCCACACGTGGGT  
ACTGTTAAGAATGGATCTGGAGACATGATATTTGAGGGAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCT  
ACCCGTCCCCATGGTGGCCCGCTACATCCGCATAAACCTCAGTCTGGTTTGATAATGGGAGCATCTGCATGA  
GAATGGAGATCCTGGGCTGCCACTGCCAGATCCTAATAATTATTATCACCGCCGGAACGAGATGACCACCACT  
GATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCAGTTGATGAAAGTTGTGAATGAAATGTGTCC  
CAATATCACAGAATTTACAACATTGAAAAAGCCACAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATC  
ACCTTGGGAGCATGAAGTCGGTGAGCCCGAGTTCCACTACATCGCGGGGGCCACGGCAATGAGGTGCTGGGC  
CGGGAGCTGCTGCTGCTGCTGGTGAGTTTCGTGTGTGAGGAGTACTTGGCCCGGAATGCGCGCATCGTCCACCT  
GGTGGAGGAGACGCGGATTACGTCCTCCCTCCCTCAACCCGATGGCTACGAGAAGGCTACGAAGGGGGCT  
CGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCACGATGGAATTGACATCAACAACACTTTCTGATTTA  
AACACGCTGCTCTGGGAGGCAGAGGATCGACAGAATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCC  
TGAGTGGTTTCTGTGCGAAATGCCACGGTGGCTGCCGAGACCAGAGCAGTCATAGCCTGGATGGAAAAATCC  
CTTTTGTGCTGGGCGGCAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCCC  
TGGAAGACGCAGGAACACACCCCCACCCCGATGACCACGTGTTCGCTGGCTGGCCTACTCCTATGCCTCCAC  
ACACCGCTCATGACAGACGCGGAGGAGGGTGTGCCACAGGAGGACTTCCAGAAGGAGGAGGGCACTGTCA  
ATGGGCGCTCCTGGCACACCGTCGCTGGAAGTCTGAACGATTCAGCTACCTTCATACAACTGCTTCGAAGT  
TCCATCTACGTGGGCTGTGATAAATACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGAATC  
TCTGATCGTGTTCATGGAGCAGGTTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTCAATGGAAAAATCC  
CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGAGTTACTGGCGCTC  
CTGAACCTGGAGAGTATGTGGTCACAGCAAAGGCCGAAGTTTCACTGCATCCACCAAGAACTGTATGGTTGG  
CTATGACATGGGGGCCACAAGGTGTGACTTCACACTTAGCAAAACCAACATGGCCAGGATCCGAGAGATCATGG  
AGAAGTTTGGGAAGCAGCCCGTCAGCCTGCCAGCCAGGCGGTGAAGCTGCGGGGGCGGAAGAGACGACAGCGT  
GGGTGACCCCTCCTGGGCCCTTGAGACTCGTCTGGGACCCATGCAAATTAAACCAACCTGGTAGTAGCTCCATAG  
TGGACTCACTCACTGTTGTTTCTCTGTAATTCAAGAAGTGCTGGAAGAGAGGGTGCAATTGTGAGGCAGGTCC  
CAAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTTCTTTGTTCCCATTTATCCAAATAACTTGGACAGAGCA  
GCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCCAACCTGGGAATCAGAGAGAGAAGGAGAAGGAGGG  
GAGCCTGTCCGTTAGAGCCTCTGGCTGCATAGAAAAGGATTCTGGTGCTTCCCCTGTTTGGCTGGCAGCAAGG  
GTTCCACGTGCATTTGCAATTTGCACAGCTAAAATTGCAGCATTTCCCCAGCTGGGCTGTCCCAATGTTACCA  
TTTGAGATGCTCCCAGGCGTCTAAGAGAATCCACCTCTCTGGCCCTGGGACATTGCAAGCTGCTACAAATAA  
ATTCTGTGTTCTTTTGACAAATAGCGTCATTGCCAAGTGACATCAGTGAGCCTCTTGAATCTGTTAGTCTCCT  
TTTTCAACAAAGGAGTGTGTTTCAGAAAAGGAGAGAGAGGCTGAGATCATTAGGAGTTTGTGGGAGCAAGCA  
TGGAGCTTCTTGACAAATTTCTGGGTCCATAAACAACCCCCAAAGTCCCTGCTGATCCAGTAGCCCTGGAGGTT  
CCCCAGGTAGGGAGAGCCAGAGGTGCCAGCCTTCTGAAGGGCCAGAAAATTTAGCCTGGATCTCCTCTTTTAC  
CTGCTAGGACTGGAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTCTCTGCTTGGGTATTGCCCTGTGTG  
GAATTGAGTGCTCATGGGTTGGCCTCATATCAGCCTGGGAGTTATTTTGTATGTAGAATGCCAGATCTTCCA  
GATTAGGCTAAATGTAATGAAACCTCTTAGGATTATCTGTGGAGCATCAGTTTGGGAAGAAATTATTGAATTAT  
CTTGCAAGAAAAGTATGTCTCACTTTTTGTTATGTGCTGCCTCATTGACCTGGGAAAAATGAAAAAAA  
AATAAAGCAAATGGTAAGACCTTAAAAA

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**FIGURE 36**

MSRPGTATPALALVLLAVTLAGVGAQGAALEDPDYYGQEIWSREPYARPEPELETFSPPLP  
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHS  
VRVAREDVRESCPPLGLETCLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA  
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIF  
EGNSEKEIPVLNELPVPVMVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT  
TDDLD FKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF  
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLP SLNPDGYEKAYEGG  
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA  
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSAST  
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES  
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRL  
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTL SKTNMARIREIMEKFGKQPVSLPARR  
LKLGRGRRRQRG

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**FIGURE 37**

CTAAGAGGACAAGATGAGGCCCGGCCTCTCATTCTCTTAGCCCTTCTGTTCTTCCTTGCCCAAGCTGCAGGGG  
ATTTGGGGGATGTGGGACCTCCAATTCACAGCCCCGGCTTCAGCTCTTTCCAGGTGTTGACTCCAGCTCCAGC  
TTCAGCTCCAGCTCCAGGTCCGGCTCCAGCTCCAGCCGAGCTTAGGCAGCGGAGGTTCTGTGTCCAGTTGTT  
TTCCAATTTACCGGCTCCGTGGATGACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTC  
CCGTGGACAGAGTGGAAACGCTTGGAAATTCACAGCTCATGTTCTTCTCAGAAGTTTGAGAAAGAACTTTCTAAA  
GTGAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAACTGTAAACCTAACTGTCCGAATTGACATCAT  
GGAGAAGGATACCATTTTCTTACACTGAACTTCGAGCTGATCAAGGTAGAAGTGAAGGAGATGGAAAAAC  
TGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAAGCTCAGAAATTTGTTGACCAGCTGGAGGTGGAGATAAGAAAT  
ATGACTCTCTTGGTAGAGAAGCTTGAGACACTAGACAAAAACAATGTCCTTGCCATTCGCCGAGAAATCGTGGC  
TCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAAACACCCCTGTCTGCCACCTCCTCCCACTC  
CAGGGAGCTGTGGTTCATGGTGGTGTGGTGAACATCAGCAAAACCGTCTGTGGTTTCAGCTCAACTGGAGAGGGTTT  
TCTTATCTATATGGTGTCTTGGGGTAGGGATTACTCTCCCCAGCATCCAAACAAAGGACTGTATTGGGTGGCGCC  
ATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTACAACACACTGGATGATTTGCTATTGTATATAA  
ATGCTCGAGAGTTGCCGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAAC  
ATGTACAACACCGGGAATATTGCCAGAGTTAACTGACCACCAACACGATTGCTGTGACTCAAACCTCTCCCTAA  
TGCTGCTATAATAACCGCTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATGAGAATG  
GATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAACTCAATGACACCACACTT  
CAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGCTTCTAACGCCTTCATGGTATGTGGGGTTCT  
GTATGCCACCCGTACTATGAACACCAGAACAGAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGG  
GCAAACTAGACATTGTAATGCATAAGATGCAGGAAAAAGTGCAGAGCATTAACTATAACCCCTTTTGACCAGAAA  
CTTTATGTCTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAAGAGCCCCAGTAAAGCTGTTTA  
GGAGTTAGGGTGAAAGAGAAAATGTTTGTGAAAAAATAGTCTTCTCCACTTACTTAGATATCTGCAGGGGTGT  
CTAAAAGTGTGTTTCATTTTGAGCAATGTTTAGGTGCATAGTTCTACCACACTAGAGATCTAGGACATTTGTCT  
TGATTTGGTGAGTTCTCTTGGGAATCATCTGCCTCTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGA  
TTGTGAGAGGTCTAGGGGCACTGTGGGCCTAGTGAAGCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTA  
GGAATTAAGGAACCTTAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAGTC  
CTCATCCATGTAGCACCCTAATTCTTCCATGCCTGGAAGAAACCTGGGGACTTAGTTAGGTAGATTAATATCT  
GGAGCTCCTCGAGGGACCAATCTCCAACCTTTTTTTTCCCTCACTAGCACCTGGAATGATGCTTTGTATGTGG  
CAGATAAGTAAATTTGGCATGCTTATATATTCTACATCTGTAAAGTGCTGAGTTTTATGGAGAGAGGCCTTTTT  
ATGCATTAAATTTGACATGGCAAATAAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTCTCTC  
ATTGTCCACCTTACTAAAAGTCAGTAGAATCTTCTACCTCATAACTTCCCTTCAAAGGCAGCTCAGAAGATTAG  
AACCAGACTTACTAACCATTCACCCCCCAACCCCTTCTACTGCCTACTTTAAAAAAATTAATAGTTTT  
CTATGGAAGTATCTAAGATTAGAAAAATTAATTTTCTTAAATTTTATTATGGACTTTTATTTACATGACTCTA  
AGACTATAAGAAAATCTGATGGCAGTGACAAAGTGCTAGCATTTATTGTTATCTAATAAGACCTTGGAGCATA  
TGTGCAACTTATGAGTGTATCAGTTGTTGCATGTAATTTTTGCCTTTGTTTAAGCCTGGAACCTGTAAGAAAAT  
GAAAATTTAATTTTTTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGT  
TGGAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTGAATGACTTTATCATCTAGTCTTTGTCTATTTT  
TCCTTTGATGTTCAAGTCTAGTCTATAGGATTGGCAGTTTAAATGCTTTACTCCCCCTTTTAAATAAATGAT  
TAAATGTGCTTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 38**

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSFPGVDSSSSFSSSSSRGSSSSSRSLGS  
GGSVSQFLFSNFTGSVDDRGTCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV  
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ  
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH  
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHHPNKGLYWVAPLNTDGRLLLEYRLYNTLD  
DLLLYINARELRITYGQSGTAVYNNNMYVNMVNTGNIARVNLTNTIAVTQTLPNAAAYNNR  
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDDTLQVLNTWYTKQYKPSASNAF  
MVCGLVLYATRTMNTRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG  
YLLNYDLSVLQKPQ



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**FIGURE 39**

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTCGTCCAC  
CCTCCTCCCACTCCAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT  
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC  
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG  
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT  
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAATGTACGTCAACA  
TGTACAACACCGGGNATATTGCCAGAGTTAACCTGACC



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**FIGURE 40**

TCTCGCAGATAGTAAATAATCTCGGAAAGGCGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT  
CCGCTGCTCTTGTGACGTTGTGGAGATGGGGAGCGTCCTGGGGCTGTGCTCCATGGCGAGCT  
GGATACCATGTTTGTGTGGAAGTGCCCCGTGTTTGCTATGCCGATGCTGTCTAGTGGAAAC  
AACTCCACTGTAAGTAGATTGATCTATGCACTTTTCTTGCTTGTGGAGTATGTGTAGCTTG  
TGTAATGTTGATACCAGGAATGGAAGAACAAGTGAATAAGATTCCTGGATTTTGTGAGAATG  
AGAAAGGTGTTGTCCCTTGTAAACATTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT  
GGTTTGGCTATGTTCTATCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA  
TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA  
TTATTGGGGCATTCTTCATTCCAGAAGGAACTTTTACAAGTGTGTGGTTTTATGTAGGCATG  
GCAGGTGCCTTTTGTTCATCCTCATACAAGTCTTACTTATTGATTTTGCACATTCATG  
GAATGAATCGTGGGTGAAAAAATGGAAGAAGGGAAGTCTGAGATGTTGGTATGCAGCCTTGT  
TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCTGTTCTTTGTCTAC  
TACACTCATCCAGCCAGTTGTTTCAGAAAAACAAGGCGTTCATCAGTGTCAACATGCTCCTCTG  
CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT  
TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT  
GAACCAGAAACAAATTGCAACCCAAAGTCTACTAAGCATAAATTGGCTACAATACAACAAGCAC  
TGTCCTCAAAGGAAGGCGAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC  
TCTTTTGTGTGTGTATTTTATTCCAGCATCCGTAAGTCTTCAAACAATAGTCAGGTTAATAAA  
CTGACTCTAACAAGTGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGAATGGATC  
ACTGGAGGATGGGGACGATGTTACCGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA  
GTTATTCCTTCTTTCATTCATGCTTTTCTGGCTTCACTTTATATCATGATGACCCTTACC  
AACTGGTCCAGGTATGAACCTCTCGTGAGATGAAAGTCAAGTGGACAGCTGTCTGGGTGAA  
AATCTCTTCCAGTTGGATTGGCATCGTGTATGTTTGGACACTCGTGGCACCCTTGTTC  
TTACAAATCGTGATTTTGAAGTGAAGTCTAGCATGAAAGTCCCACTTTGATTATTGC  
TTATTTGAAACAGTATTTCCCACTTTTGTAAAGTTGTGTATGTTTTGCTTCCCATGTAAC  
TTCTCCAGTGTCTGGCATGAATTAGATTTTACTGCTTGTCAATTTTGTATTTTCTTACCAA  
GTGCATTGATATGTGAAGTAGAATGAATTGACAGGAAAGTTTATGAATATGGTGAATGAGT  
TAGTAAAAGTGGCCATTATTGGGCTTATTCTGCTCTATAGTTGTGAATGAAGATAAATA  
ACAAATTTGTTTGAAGTATTTTAAATATATTAGACCTTAAGCTGTTTTAGCAAGCATTAAA  
GCAAATGTATGGCTGCCTTTTGAATATTTGATGTGTGCTTGGCAGGATACTGCAAAGAAC  
ATGGTTTATTTTAAATTTTATAAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA  
AGTTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTGTTAGTGGACAATAGTGTAG  
TTATGGATGGAGGTGTCGGTACTAAATTGAATAACGAGTAAATAATCTTACTTGGGTAGAGA  
TGGCCTTTGCCAACAAAGTGAAGTGTGTTTGGTTGTTTAAACTCATGAAGTATGGGTTTCACT  
GGAAATGTTTGGAACTCTGAAGGATTTAGACAAGGTTTGAAGGATAATCATGGGTTAGA  
AGGAAGTGTGTTGAAAGTCACTTTGAAAGTTAGTTTTGGGCCAGCAGGATAGCTCACCCTT  
GGTAATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCAGGAATTCAGACCA  
GCTTGGCACATGGTGAACCTGTTCTATAAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTC  
CAGCACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAAGCAAGTCA  
CGTCACTGCACTCTAGCTGGCACAGAGTAAGCCAAAAAATATATATATATTGAAATCAAGG  
AGGCAAAATTTTGAAGGGAAGGAAGTAACTGCAAAACCACTAGGCTTTAGTAGGTACTTAT  
ATAAAATCTAGTCCAGTTCTCTCATTTAAAAAATGAAGACACTGAAATACAGACTTAAATA  
GCTCAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTGACATTTAA  
AAATAATTTCTATTCAAATACATGCATATTGATTTACACCTCATACTGTGATAATTAATGT  
GATGTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTCAGAAGAATGATGGAATGTTTT  
AGAATAAACTCCTGCTTATAGTATACTACACAGTTCAAAAGATGTTTAAATGCTTTTGTAT  
TTACTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAATCAAGCAGT  
ATGAGAGTTTGTATTTGTATGTGTCACTAGTGTCTAATGAAGCTTTTAAATCTACAATT  
TCTTCTTTAAAAATATTTATTAATGTGAATGGAATATAACAATTCAGCTTAATCCCCAAC  
TTATTCTGTGTGTAGACATTGTATCCACAATTTTGAATGGCTGTGTTTTACCTCTAAATAA  
ATGAATTCAGAGAAAAA

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**FIGURE 41**

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME  
EQLNKIPGFCENEKGVVPCNILVGKYKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG  
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQVLVLLIDFAHSWNESWVEKM  
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI  
LPKIQESQPRSGLLQSSVITVYTMYLTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV  
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH  
RAVDNERDGVITYSYFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVVVKISSSWIGI  
VLYVWTLVAPLVLTNRDFD

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**FIGURE 42**

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT  
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCC  
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACAANTCCACTGTAACTAGATTGATCTA  
TGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG  
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT  
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCT  
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT  
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

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**FIGURE 43**

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC  
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAACAANTCC  
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT  
GTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG  
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG  
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG  
AGCTGCAGTGCACAATGGATTTTGGTTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG  
GGGC

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**FIGURE 44**

AAGAAGCTGTCTCCATCTTGTCTGTATCCGCTGCTCTTGTGAACGTTNTGGAGATGGGGAGC  
GTCCTTGGGGTTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCCCCGTGTT  
TGCTATGCCGATGCTGTCCTAGTGGAAACAACCTCCACTGTAAC TAGATTGATCTATGCACTT  
TTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAAC  
GAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATTTTGGTTG  
GCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTTTA  
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTT  
CTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

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**FIGURE 45**

GCTGTCCTTAGTGGAAACAANTCCAACCTGTAACCTGGATTGATCTATGCACTTTTTTCCTTG  
CTTGTTGGAGTATGTGTAGCTTTGTGTAATGTTGTTCCCAGGATTGGANGAACAACTGAATA  
AGATTCCTGGATTTTTGTGAGAATGAGAAAGGTGTTGTCCCCTTGTAACATTTTTGGTTGGC  
TATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTCTCTCTTTACT  
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCT  
TTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTTCATTCCAGAAGGAACCTTT  
ACAACTGTGTGGTTTTATGTAGGCATGGCAGGTGCCTTTTGTTCATCCTCATACAACTAGT  
CTTACTTATTGATTTTGCACATTCATGGAATGAATCGTGGGTGAAAAAATGGAAGAAGGGA  
ACTCGAGATGTTGGTATGCAGCCTTGTTATCAGCTACAGCTCTGAATTATCTGCTGTCTTTA  
GTTGCTATCGTCCTGTTCTTTGTCTACTACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGC  
GTTTCATCAGTGTCAACATGCTCCTCTGCGTTGGTGCTTCTGTAATG

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**FIGURE 46**

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCTGCGATTGAGCTGCGGGTTCGCGGCCGCGCGCCCTCTCCAAT  
GGCAATGTGTGTGGCTGGAGGCGAGCGGAGGCTTTTCGGCAAAGGCAGTCGAGTGTTCGACAGCCGGGGCGAG  
TCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGTGTCTATTACGAGGGGAGCGCCCGCGGGGCTGTGCG  
ACTCCCCGCGGAACATTTGGCTCCCTCCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAGAGGCAGATTAC  
GTCGTTTCCAGCCAAGTGGACCTGATCGATGGCCCTCCTGAATTTATCACGATATTTGATTTATTAGCGATGCC  
CCCTGGTTTGTGTGTTACGCACACACACGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGTTTCCAGCTCC  
TGGGCGAATCCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGAGAGTGTGTGCAATCTGCGAGTG  
AAGAGGGACGAGGGAAAAGAAACAAAGCCACAGACGCAACTTGAGACTCCCGCATCCCAAAAGAACACCAGAT  
CAGCAAAAAAAGAAGATGGGCCCCCCGAGCCTCGTGCTGTGCTTGTGCTCGCAACTGTGTTCTCCCTGCTGGG  
TGGAAGCTCGGCCTTCTGTGCGCACCACCGCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCCA  
ACATCATCCTGGTGCTGACGGACGACCAGGATGTGGAGCTGGGTTCCATGCAGGTGATGAACAAGACCCGGCGC  
ATCATGGAGCAGGGCGGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATGTGCTGCCCTCACGCTCCTC  
CATCCTCACTGGCAAGTACGTCCACAACCACAACCTACACCAACAATGAGAACTGCTCCTCGCCCTCCTGGC  
AGGACAGCAGCAGAGAGCGCACCTTTGCCGTGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAG  
TATCTTAATGAATACAACGGCTCTACGTGCCACCCGGCTGGAAAGGAGTGGGTGCGGACTCCTTAAAAACTCCCG  
CTTTTATAACTACACGCTGTGTGGAACGGGGTGAAGAGAAGCACGGCTCCGACTACTCCAAGGATTACCTCA  
CAGACCTCATCACCATGACAGCGTGAGCTTCTTCGCGACGTCCAAGAAGATGTACCCGCACAGGCCAGTCCCTC  
ATGGTCATCAGCCATGCAGCCCCCAGGCCCTGAGGATTACAGCCCCACAATATTCACGCCTCTTCCCAAACGC  
ATCTCAGCACATCAGCCGAGCTACAACCTACGCGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGC  
CCATGAAGCCCATCCACATGGAATTCACCAACATGCTCCAGCGGAAGCGCTTGACAGCCCTCATGTGCGGTGGAC  
GACTCCATGGAGACGATTTACAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACACCGC  
CGACCACGGTTACCACATCGGCCAGTTTGGCCTGGTGAAGGGAAATCCATGCCATATGAGTTTGACATCAGGG  
TCCCGTTCTACGTGAGGGGCCCCAACGTGGAAGCCGGCTGTCTGAATCCCAACATCGTCCCTCAACATTGACCTG  
GCCCCACCATCCTGGACATTCGAGGCCTGGACATACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCT  
GGACACGGAGCGGCCGGTGAATCGGTTTCACTTGAAGAAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGG  
AGAGAGGCAAGCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCAGGAGGAGAACTTTCTGCCCAAGTAC  
CAGCGTGTGAAGGACCTGTGTGAGCGTGTGAGTACCAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTG  
TGTGGAGGACGCCACGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCCCATGCGGCTGGGCGGCAGCAGAGCCC  
TCTCAACCTCGTGCCCAAGTACTACGGGCAGGGCAGCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTC  
AGCCTGGCCGACGCCGGAAGAACTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCG  
CTCAGTGGCCATCGAGGTGGACGGCAGGGTGTACACGTAGGCTGGGTGATGCCGCCAGCCCCGAACCTCA  
CCAAGCGGCACTGGCCAGGGGCCCTGAGGACCAAGATGACAAGGATGGTGGGGACTTCAGTGGCACTGGAGG  
CTTCCCGACTACTCAGCCGCCAACCCATTAAAGTGACACATCGGTGCTACATCCTAGAGAACGACACAGTCCA  
GTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGAAAGACCACAAGCTGCACATCGACCACGAGATTGAAA  
CCCTGCAGAACAAATTAAGAACTGAGGGAAGTCCGAGGTACCTGAAGAAAAGCGGCCAGAAGAATGTGAC  
TGTCACAAATCAGCTACCACCCAGCACAAAGGCCGCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTTCAG  
GAAGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAACTCCGCAAGCTGC  
TCAAGCGCCTGCAGAACACGACACGTGCAGCATGCCAGGCCTCACGTGCTTACCCACGACAACCAGCACTGG  
CAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGCTGCACCAGCGCCAACAATAACAGTACTGGTGCAT  
GAGGACCATCAATGAGACTACAATTTCTCTTCTGTGAATTTGCAACTGGCTTCTAGAGTACTTTGATCTCA  
ACACAGACCCCTACCAGCTGATGAATGCAGTGAACACACTGGACAGGGATGTCTCAACCAGCTACACGTACAG  
CTCATGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAAACCCCGGACTCGAAACATGGACCTGGATGGAG  
AAGCTATGAGCAATACAGGCAGTTTCAGCGTGCAGAGTGGCCAGAAATGAAGAGACCTTCTTCCAAATCACTGG  
GACAACCTGTGGGAAGGCTGGGAAGGTTAAGAAACACAGAGGTGGACCTCCAAAAACATAGAGGCATCACCTGA  
CTGCACAGGCAATGAAAAACCATGTGGGTGATTTCCAGCAGACCTGTGCTATTGGCCAGGAGGCCTGAGAAAGC  
AAGCAGCACTCTCAGTCAACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCC  
ATTTTTGCCCTGCTTTTGTGTTGATTATACCTACCAGCTGCACAAATGCATTTTTTCGTATCAAAAAGTC  
ACCAATAACCTCCCCAGAAGCTCACAAGGAAAACGGAGAGAGCGAGCGAGAGATTTCTTGGAAATTTCT  
TCCCAAGGGCGAAAGTCATTGGAATTTTAAATCATAGGGGAAAAGCAGTCTGTTCTAAATCCTTATTCTT  
TTGGTTTGTACAAAGGAAGGAACTAAGAAGCAGGACAGGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACG  
TTTGACAATGAGTCAGTAGCACAAAGAGATGACATTTACCTAGCACTATAAACCTGGTTGCTCTGAAGAAA  
CTGCCTTCATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACTTTTAGGGGAACCTAATAAGAAAT  
CCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAGAAAAA

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**FIGURE 47**

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRDRRNIRPNIILVLTDDQDVELGSMQ  
VMNKTRRIMEQGGAHFINAFVTTMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHE  
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD  
YSKDYLTDLITNDSVSFFERTSKKMPHRPVL MVISHAAPHGPEDSAPQYSRLFPNASQHITP  
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT  
YIVYTADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI  
AGLDIPADM DGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN  
FLPKYQRVKDLQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKY  
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSV AIEVDGRVYHVGLGDAAQ  
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQC DL DLYKS  
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSL  
HPFRKGLQEKDKVWLLREQKRKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG  
PFCACTSANNNTYWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDV LNQL  
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG



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**FIGURE 48**

AACAAAGTTCAGTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA  
GCTGCTGGGCAGAGAGGGGACTGTCCGGCTCCCAGATGCTGGGCCTCCTGGGGAGCACAGCCC  
TCGTGGGATGGATCACAGGTGCTGCTGTGGCGGTCTGCTGCTGCTGCTGCTGCTGGCCACC  
TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGAAA  
CCGAGTCCGCCGGGCCAGCCTTGGCCCTTCCGGCGGCGGGGCCACCTGGGAATCTTTCACC  
ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC  
CCCCGCCACACCCCTCACCACCTCCACCACCACCACCACCCCCACCGCCACCATCCCCGCCA  
CGCTCGCTGAGGCTGCTGTGCGCCGGTGCCTGTGGACAGCAGCTGCCCCTGCCCTCCCATCTG  
TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG  
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTAATGAGG  
AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG  
GTGCTCTTTCGGGGCTGGACAGCCCGTCTTGTGACAGTGAAGTCCCAGTGAGCCCCAGAAATG  
ACAAGCGTGTCTTGGCAGAGCCAGCACACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC  
ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT  
GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT  
AAAAACCACTAAGAAGCTTTAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 49**

MLGLLGSTALVGWITGAAVAVLLLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRRAQWPFR  
RRGHLGIFHHHRHPGHVSHVFPNVGLHHHHHPRHTPHHLHHHHHPRHHPRHAR

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**FIGURE 50**

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCCATGTCGGACCTGCTA  
CTACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTGCCGG  
GTACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTACCCCCCATCCGCAACGTCA  
CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC  
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC  
CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC  
CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC  
CATGTGGTGACAGCCACCTTCCCCTACACCACCATTTCTGTCCATCTGGCTGGCTACCCGCCG  
TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG  
AGATCTACCAGGAAGACCAGATCCATTTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTAT  
GTGCCTGAGATGAAGGAGACAGAGTGGAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA  
GGTGGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCC  
CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCAGCCGTGGCTGGGAT  
GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA  
GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGC  
CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAGTAACCC  
ATGGCCTGCACCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT  
CCAGCCCTCTTCCTCCTTCTCTGGGGGAGGAGGGGTTCTGAGGGACCTGACTTCCCCTGC  
TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA  
GGGACTATTTTCTGCACCAGCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTCAGACTC  
ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAA  
AAAAA

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**FIGURE 51**

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGlyGETGR  
LFTESCSISPKLRSIAVYYDNPHMVPPDKCRAVGSI LSEGEESPSPELIDLYQKFGFKVFS  
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCLAR  
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAA TLSPGAS  
SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGLGESRLDPGTEPLGTTKWLWEPTAPEK  
GKE

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**FIGURE 52**

CCGCGGGAACGCTGTCCTGGCTGCCGCCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCT  
GCCCCGCGCCCAGTCATGACCCTGCGCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCT  
GCTGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGA  
CCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGA  
GACACGCTTCACATACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCT  
GACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGA  
GTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTAT  
GGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCT  
GATTGCACTAATCCGAGCCAACCTACTGGCTAAAGCTGGTGAAGGGCATTTTGCCTCTGGTAG  
GGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAAT  
AGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAATA  
ATAAATAATAAATTTTAAAAAACTTAAAAAAAAAAAAAAAAAAAA

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**FIGURE 53**

MTLRPSLLPLHLLLLLLLLLSAAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGDTLHI  
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF  
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS  
KKKLKEEKRNKSKKK

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**FIGURE 54**

CCCGGGAACGTGTTCCCTGGCTGCCGCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCTGC  
CCCGCGCCCAGTCATGACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCTGC  
TGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGACC  
CTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGAGA  
CACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCTGA  
CCAGAGACCCTCTGGTTATAGAAGCTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT  
CTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTATGG  
AAAACGGGGATTTCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCTGA  
TTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTCTTGCCTCTGGTAGGG  
ATGGCCATGGTGCCACCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAATAGA  
CCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAAATAATA  
AATAATAAATTTTAAAAAACTTA

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**FIGURE 55**

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC  
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG  
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA  
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT  
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT  
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGG  
GCATTTTGCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC  
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAA  
CAAGAGCAAAAAGAAATAATAAATAATAAATTTTAAAAAACTTAAAA



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**FIGURE 56**

CTGCTGCATCCGGGTGTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAATCGGGGGAG  
TGAGGCGGGCCGGCGCGGCGGACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG  
ACCTGAAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG  
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT  
TATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGATTTC AACCACTCATACCATGCCT  
GTGGTGTTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA  
GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG  
TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG  
CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT  
TTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGACTTATGGCAGTGAACACATCTGAT  
TTCCACAGCACAAACAGCCCTGCATGGGTTTGTGTTTTTTTACTGCTCACTCCCAACCTT  
TTGTAATGCCATTTTCTAAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT  
AAAATCACGAGAACACCTAAACAACAACCAAAATCTATTGTGGTATGCACTTGATTAACCTT  
ATAAAATGTTAGAGGAACTTTCACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT  
TGTA AAAATAAAAAGAAATTACAAAAGAAATTATGGATTTGTCAATGTAAGTATTTGTCATA  
TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT  
CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAATATTCCGTGG  
TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAATTTCTGTGAACATGTAAT  
GTA ACTGGCTTTTGAGGGTCTCCCAAGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT  
GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTCCGCTGTGCCTCTCAT  
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTTCTGGTGGGATGCACAGTCACTC  
CACATCCACCACTG

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**FIGURE 57**

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWIIIDA AVIYPTMKDFNHSYHACGVI  
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK  
DIVYPGIAVFFQNAFIFFGGLVEKFGRTEDLWQ

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**FIGURE 58**

TTCTTGGCTAAAATCGGGGGAGTGAGGCGGGCCGGCGCGGCGGACACCGGGCTCCGGAACC  
ACTGCACGACGGGGGCTGGACTGACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATG  
CTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC  
TATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGAT  
TTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGC  
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTG  
CTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGG  
ATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATT  
TTTCCAGAATGCCTTCATCTTTTTTTGGAGGGCTGGTTTTTAAGTTTGGC

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**FIGURE 59**

TGGACGGACCTGAAAAAATGTTTGGATTNTAGAGGGNTTGAGATG TTCAGAATGCATGAC  
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG  
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC  
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA  
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTTGGCTTTT  
CGTTGGTTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT  
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC  
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

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**FIGURE 60**

GGACACCGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAATGTTTGGATT  
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT  
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT  
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGC  
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT  
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT  
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT  
ACCCTGGAATTNCTNTATTTTTTCCAGAATGCC

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**FIGURE 61**

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC  
ATTGNTGNTGGTGTANTATTTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT  
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC  
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG  
TTTGGGTCAAACAGGTGNTNGCATTTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN  
TGATTGCATTTATGTGGATTNTTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC  
CCTGT

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**FIGURE 62**

GGGAGGCTGTGNCCGTTTTGTTTTNTTGGCTAAAATCGGGGGAGTGAGGCGGCCCGGCGCGG  
CGNGACACCGGGTTCCGGGAACCATTGCACGACGGGGTGGACTGACCTGAAAAAATGTTTG  
GATTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATT  
GCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT  
TATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCA  
TAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA  
GGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGG  
ATNTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAG  
TATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATNTTTTTTGGAGGGCTG

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**FIGURE 63**

CGACGCCGGCGTGATGTGGCTTCCGCTGGTGCTGCTCCTGGCTGTGCTGCTGCTGGCCGTCC  
TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC  
AAACGGCCCCCAGCGCCCCCTGGTAAGTACAAAGGAGGCCAGGAAGAAGGTTCTCAAACAAGC  
TTTTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG  
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGCTGGAACAACAT  
ACCAAGGCAGGGGGGCTGCTGTCATACCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT  
CCATTACATTGGGCGTATGGAAGAGGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG  
AAGGGCAGCTGGACTGGGCTCCCCTGTCTCTCCTTTTGACATCATGGTACTGGAAGGGCCC  
AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTCAGGGCCTCAAGGA  
GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA  
GTGGAGCCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTTGCCCGTGGTTTACAGTCTCTCGAC  
AGGTGTGGGCTGCTGACTCGTTTCTCTCCATTCTTCAAGCATCCACCCAGAGCCTGGCTGA  
GGTCTTGACAGCAGCTGGGGGCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA  
CTTACGGTGTACCCCCAACCACAGTGCCTTTTCCATGCACGCCCTGCTGGTCAACCACTAC  
ATGAAAGGAGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT  
GATTCAGCGGGCTGGGGGCGCTGTCTCACAAAGGCCACTGTGCAGAGTGTGTTGCTGGACT  
CAGCTGGGAAAGCCTGTGGTGTGAGTGTGAAGAAGGGGCATGAGCTGGTGAACATCTATTGC  
CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTATGCCGGGGAACGC  
CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGGCGCCGGGCTTAGGCATGACCT  
CTGTTTTCTATCTGCCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT  
GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCCAGGGGAAGA  
GGTGGCGGAACACATCCCTCTTCTTCTTCTCGCTTCCCATCAGCCAAAGATCCGACCTGGG  
AGGACCGATTCCCAGGCCGGTCCACCATGATCATACCCACTGCCTACGAGTGGTTT  
GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGGCAGTGACTATGAGACCTTCAAAAACCTC  
CTTTGTGGAAGCCTCTATGTGAGTGGTCTGAAACTGTTCCACAGCTGGAGGGGAAGGTGG  
AGAGTGTGACTGCAGGATCCCCACTCACCAACCAGTTCTATCTGGCTGCTCCCCGAGGTGCC  
TGCTACGGGGCTGACCATGACCTGGGCCGCTGCACCTTGTGTGATGGCTCTCTTGAGGGC  
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTACCTGTGGAGTGGTCTG  
GGGCCCTGCAAGGTGCCCTGCTGTGACAGCGCCATCCTGAAGCGGAACCTGTACTCAGAC  
CTTAAGAATCTTGATTCTAGGATCCGGGCACAGAAGAAAAAGAATTAGTTCCATCAGGGAGG  
AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG  
CATTAGTTCCCTTGCACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCTAG  
TTTAAATCACAATTCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA  
TCTTTACGCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG  
TCTCATGACGAGCGGCGCTCTGCATCCCTCACCCTGCCTCCTAACTCAGTGATCAAAGCGA  
ATATTCCATCTGTGGATAGAACCCCTGGCAGTGTTGTGCTCAGCTCAACCTGGTGGGTTTCACTT  
TGTCCTGAGGCTTCTGCTCTCATTCTTTAGTGCTACGCTGCACAGTTCTACATGTCAAGG  
GAAAAGGGAGACTAATGAGGCTTAACCTCAAACCTGGGGCTGGTTTTGGTTGCCATTCCATA  
GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTTCACTGGCTCTTTCAGGGGACAGGAAAT  
GCCTGTGTCTGGCCAGTGTGGTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA  
GGGTGCATGTGAGATGATCATATCCAATTCATATGGAAGTCCCGGGTCTGTCTTCTTATCA  
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGGACTCAGTACCTGAGCCTCAATCAAGC  
CTTATCCACCAATAACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA  
TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG  
CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAGGGAAGTCACATCAGAAAAGGGA  
AAGCCACGGAATGTGTGTGAAGCCAGAAATGGCATTTCAGTTAATTAGCACATGTGAGGG  
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTCAGTTATGTCTTTG  
GTATCAGACATACGAAAGGTCTCTTTGTAGTTTCGTGTTAATGTAACATTAATAAATTTATTG  
ATTCCATTGCTTTAAAAA



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**FIGURE 64**

MWLPLVLLLAVLLLAVLCKVYLGLFSGSSPNPFSEDVKRPPAPLVTDKARKKVLKQAFSAN  
QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG  
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ  
EEAIIIDKYIKLVKVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ  
LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA  
GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP  
GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVYYDTMDQAMERYVSMPREEAAEH  
IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAELKGKRGSDYETFKNSFVEA  
SMSVVLKLFQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI  
PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

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**FIGURE 65**

[illegible]

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**FIGURE 66**

MRVRIGLTLLLCVLLSLASASSDEEGSQDES LDSKTTLTSDSVKDHTTAGRVVAGQIFLD  
SESELESSIQEEEDSLKSQEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG  
EPCHF PFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEEAKRRQMQEAMM  
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERSYALLFGDYLPQNIQAAREMF EK  
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLI AHMVLVSRL

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**FIGURE 67**

CTTCCCAGCCCTGTGCCCCAAAGCACCTGGAGCATATAGCCTTGCAGAACTTCTACTTGCCT  
GCCTCCCTGCCTCTGGCCATGGCCTGCCGGTGCCTCAGCTTCCTTCTGATGGGGACCTTCCT  
GTCAGTTTCCCAGACAGTCCTGGCCCAGCTGGATGCACTGCTGGTCTTCCCAGGCCAAGTGG  
CTCAACTCTCCTGCACGCTCAGCCCCCAGCAGTCACCATCAGGGACTACGGTGTGTCCTGG  
TACCAGCAGCGGGCAGGCAGTGCCCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA  
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCCAACAATGCCT  
GTGTCCTCACCATTAGTCCCGTGCAGCCTGAAGACGACGCGGATTACTACTGCTCTGTTGGC  
TACGGCTTTAGTCCCTAGGGGTGGGGTGTGAGATGGGTGCCTCCCCTCTGCCTCCCATTCT  
GCCCCTGACCTTGGGTCCCTTTTAAACTTTCTCTGAGCCTTGCTTCCCCTCTGTAAAATGGG  
TTAATAATATTCAACATGTCAACAAC

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**FIGURE 68**

MACRCLSFLLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG  
SAPRYLLYYRSEEDHHRPADIPDRFSAAKDEAHNACVLTISPVQPEDDADYYCSVGYGFS

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**FIGURE 69**

GCCGCCCCGCCCCGAGACCGGGCCCCGGGGGCGCGGGGCGGCGGGATGCGGGCGCCCCGGGGCGG  
CGATGACCCGCGGAGCGCACGCGCGGGCCCCGCCCCCTGACCCCGCCCCGCCCCGCTGAGCCCC  
CCCGCCGAGGTCCGGACAGGCCGAGATGACGCGCGAGCCCCCTGTTGCTGCTCCTGCTGCCGC  
CGCTGCTGCTGGGGGCCTTCCCACCGGCCGCGCGCCCCGAGGCCCCCAAAGATGGCGGAC  
AAGGTGGTCCCACGGCAGGTGGCCCCGCTGGGCGCAGTGTGCGGCTGCAGTGGCCAGTGGGA  
GGGGGACCCGCGCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA  
GCCGCTTCCGCGTGCTGCCGCAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC  
GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCCTGAGCGTCAACTACACCCTCGTCTG  
GCTGGATGACATTAGCCCAGGGAAGGAGAGCCTGGGGCCCCGACAGCTCCTCTGGGGGTCAAG  
AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC  
CGGGTGATCGCACGGCCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCCTGGCCAGCGGGCAGCC  
TCGGCCCCGACATCACGTGGATGAAGGACGACAGGCCTTGACGCGCCCCAGAGGCCGCTGAGC  
CCAGGAAGAAGAAGTGGACACTGAGCCTGAAGAACCCTGCGGCCGGAGGACAGCGGCAATAC  
ACCTGCCGCGTGTCGAACCGCGCGGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA  
GCGGACCCGTTCCAAGCCCGTGCTCACAGGCACGCACCCCGTGAACACGACGGTGGACTTCG  
GGGGGACCACGTCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG  
AAGCGCGTGGAGTACGGCGCCGAGGGCGCCACAACCTCCACCATCGATGTGGGCGGCCAGAA  
GTTTGTGGTGCTGCCACGGGTGACGTGTGGTTCGCGGCCGACGGCTCCTACCTCAATAAGC  
TGCTCATCACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCTTGCGCCAAACACC  
ATGGGCTACAGCTTCCGCAGCGCCTTCCTACCCGTGCTGCCAGACCCAAAACCGCCAGGGCC  
ACCTGTGGCCTCCTCGTCTCGGCCACTAGCCTGCCGTGGCCCCGTGGTTCATCGGCATCCCAG  
CCGGCGCTGTCTTATCCTGGGCACCCCTGCTCCTGTGGCTTTGCCAGGGCCAGAAGAAGCCG  
TGACCCCCCGCCCTGCCCTCCCTGCTGGCGACCGCCCGCCGGGGGACCGCGCAGCCG  
CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGTGTGGGGCTGT  
GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCCAGTTGCTGGC  
CCTAAGTTGTACCCCAAACCTCTACACAGACATCCACACACACACACACACTCTCACAC  
ACACTCACACGTGGAGGGCAAGGTCCACCAGACATCCACTATCAGTGCTAGACGGCACCGT  
ATCTGACGTGGGCACGGGGGGCGGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT  
GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCAGGCAGTCTGTGTG  
TGAGGCATAGCCCCTGGACACACACACACAGACACACACACTACCTGGATGCATGTATGCAC  
ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG  
CCGCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA  
TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGCTGCCTGGACA  
CACACACACACACGGATATGCTGTCTGGACGCACACACGTGCAGATATGGTATCCGGACACA  
CACGTGCACAGATATGCTGCCTGGACACACAGATAATGCTGCCTTGACACACACATGCACGG  
ATATTGCCTGGACACACACACACACACACGCGTGCACAGATATGCTGTCTGGACACGCACAC  
ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT  
GCCTGGACACACGCAGATATGCTGTCTAGTCACACACACACGCAGACATGCTGTCCGGACAC  
ACACACGCATGCACAGATATGCTGTCCGGACACACACACGCACGCAGATATGCTGCCTGGAC  
ACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATATTGCCTGGACACACACA  
TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG  
CACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGACACACATGCACACAGGT  
GCAGATATGCTGCCTGGACACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA  
TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA  
TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA  
CACACATGCACACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTG  
GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT  
CCCTGCTCCACCGTCACTCCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC  
CATCCCCGCCTCTGTCCCCTGGCCTTGGCGGCTATTTTGGCCACCTGCCTTGGGTGCCCAGG  
AGTCCCCCTACTGCTGTGGGCTGGGGTTGGGGGACAGCAGCCCCAAGCCTGAGAGGCTGGAG  
CCCATGGCTAGTGGCTCATCCCCAGTGCATTTCCCCCTGACACAGAGAAGGGGCTTGGTA  
TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTTCAGGGAC  
TGTGGTCTCTCCTGGGGCCCCGGGACCCGCTGGTCTTTCAGCCATGCTGATGACCACACCCC  
GTCCAGGCCAGACACCACCCCCACCCACTGTCTGTGGTGGCCCCAGATCTCTGTAATTTTA  
TGTAGAGTTTGAGCTGAAGCCCCGTATATTTAATTTATTTTGTAAACACAAAA

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**FIGURE 70**

MTPSPLLLLLLPPLLLGAFPPAAAARGPPKMADKVVPQRQVARLGRTVRLQCPVEGDPPPLTM  
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDDISPGK  
ESLGPDSSSSGGQEDPASQQWARPRFTQPSKMRRRVIA RPVGSSVRLKCVASGHPRPDITWMK  
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL  
TGTHPVNTTVDFGGTTSFQCKVRS DVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD  
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLTVLPDPKPPGPPVASSSSA  
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS  
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTSHHTSHHVEGKV  
HQHIHYQC

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**FIGURE 71**

CCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAACTTCCCAGGGGACCGCATTCCAGAGTCA  
AGTGACTCTGTGAAGACCCACATCTACCTCTTGCCACGTTCCCACGGGCTGGGGGAAAGATGGTGGGGACCA  
AGGCTGGGTGTTCTCTCTCTGGTCTGGAGTACATCTGTGTTGGGGAGACAGCATGCTCACCAGTCAC  
GTAAGAAGAGTCCAGCCTGGGAAGAAGAACCCAGCATCTTTGCCAAGCCTGCCGACACCTGGAGAGCCCTGG  
TGAGTGGACAAACATGTTTCAACATCGACTACCCAGGCGGGGAAGGGCCATATGAGCGGCTGGACGCGATTGCT  
TCTACTATGGGAGCCGTGTATGTGCCCGTCCCTGCGGCTAGAGGCTGGACCACTACTGACACCTGCGGGC  
AGCACTGGCCAGGTGGTCCATGGTAGTCCCGTGAGGGTCTTGGTGCTCAACAGGGAGCAGCGGCTGGCCA  
GAATGCTCTAATTACACCGTAGCTCTCTCTGCCACACAGGATCCCTGCGCGGACACAGCAGCGCATCTGGA  
GCCATGGTCTCCCTGGAGCAAGTGCTCAGCTGCGTGTGGTCAGACTGGGCTCCAGACTGCACACGCAATTGCT  
TTGGCAGAGATGGTGTGCTGTGCACTGAGGCGCAGCGAAGAGGGTCAAGCATGCATGGGCCAGGACTGTACAGC  
CTGTGACCTGACCTGCCCAATGGGCGAGGTGAATGCTGACTGTGATGCTGCATGTGCCAGGACTTCATGCTT  
ATGGGGCTGTCTCCCTTCCCAGAGGTGCCAGCCTCAGGGGCTGCTATCTACCTCTGACCAAGACGCCAAG  
CTGCTGACCCAGACAGACAGTGTATGGGAGATTCCGAATCCCTGGCTGTGCTGCTGATGGCGAAAAGCATCCTGAA  
SATCAAAAGGTCAAGTTTGGCCCCATTGTACTCAAAATGCCAAGACTAGGCTGAAGGCAGCCACCATCAAGG  
CAGAGTTTGTGAGGGCAGAGACTCCATACATGGTGATGAACCTGAGACAAAAGCAGGAGAGCTGGGCAGAGC  
GTGTCCTGTGCTGTGAAGGCCACAGGGAAGGCCAGGCCAGACAAAGTATTTTTGGTATCATTAATGACACATTTGCT  
GGATCCTTCCCTCTACAGCATGAGAGCAAGCTGGTGCTGAGGAACTCAGCAGCACCAGCTGGGGAGTACT  
TTTGAAGGCCCAAGTAGTGTGGGGCTGTGAAGTCAAGGTTGCCAGCTGATTGTCAAGCATCTGATGAG  
ACTCCTTGCAACCCAGTCTGCTGAGAGCTATCTTATCCGGCTGCCCATGATTGCTTTCAGAATGCCACCAATC  
CTTCTACTATGACGTGGGACGCTGCCCTGTAAAGATTGTGCAAGGCAGCAGGATAATGGGATCAGGTGCCGTG  
ATGCTGTGCAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCAGTGGCTACACGCTACCC  
ACCAAGTGGGCCAAGAGTGCAGCTGCCAGCGGTGTACAGAACTCGGAGCATCGTGGCGGGCGGTGTGAGTGC  
TGCTGACAATGGGGAGCCCATCGCTTTGGCCATGTGTACATGGGGAACAGCGGTGAAGCATGACTGGCTACA  
AGGGCACTTTACCCCTCCATGTCCCCCAGGACACTGAGAGGCTGGTGCTCACATTTGTGGACAGGCTGCAGAAG  
TTTGTCAACACCCAAAGTGCTACCTTCAACAAGAAGGGAGTCCGCTGTTCCATGAAATCAAGATGCTTCG  
TCGGAAGAGCCCATCACTTTGGAGGCCATGGAGAACCAATCATCCCCCTGGGGGAAGTGTTTGGTGAAGACC  
CCATGGCTGAACCTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACATAGGAAAAGTGAAG  
CGCAGTGTGACCTTCTGGATCCCCCGGAATATTTCCACAGCCACAGCTGCCAGACTGACCTGGAACCTCATCA  
TGACGAAGGAGACATTTCCCCCTTCGGAGCTATGGCATGTTCTGTGGACTTCAGAGATGAGGTCACTCAG  
AGCCACTTAATGCTGGCAAAGTGAAGGTCACTCTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACA  
GTGAACCTCTGTGCTCAATCAACACAGCGGCTGTGGGAGGAGGAGGTGATTTCAAATTTGAAATCAAG  
GAGGAACAAAAGAGAGACAGAACCTCTCGTGGGCAACCTGGAGATTCTGTGAGAGAGGCTCTTTAACCCTGG  
ATGTTCTGAAAGACAGCGGCTGCTTTGTTAAGGTGAGGGCTACCGGAGTGAGAGTCTTCTGCTATGTGAGCAG  
CTCAGGGGGTGTGATCTCCGTGATTAACCTGGAGCTAGAACTGGCTTCTGTGCCAACCTAGGCGCTGGG  
CGCTTTGACAGTGTCAACACAGGCCCCAACGGGGCCTGTGTGCTGCTTCTGTGATGACAGCTCCCTGATG  
CCTACTCTGCTTATGCTTTGGCAAGCTGGCTGGGGAGAACTGCAAGCAGTGGAGTCTTCTCTAATTTCAAC  
CCAAATGCAATTTGGGCTCCCTCAGCCCTATCTCAACAAGGCTCACTACCGCTCGGACGACCATGAGGATCCAG  
GGTTAAAAAGACAGCTTTCCAGATTAGCATGGCCAAGCCAAGGCCAACTCAGCTGAGGAGAGCAATGGGCCCCA  
TCTATGCTTTGAGAACCTCGGGCATGTGAAGAGGCCACCCAGTGCAGCCCATTCGCGTTCTACCAAGATT  
GAGGGGATCGATATGACTACAACACAGTCCCCCTCAACGAAGATGACCTATGAGTGCAGTGAAGACTATCT  
GGCATGGTGGCCAAAGCCGATGGAATTCAGGGCCTGCTATATCAAGGTGAAGATTGTGGGGCCACTGGAAGTGA  
ATGTGCGATCCCCCAACATGGGGGCACTCATCGCGGACAGTGGGGAGCTGTATGGAATCCGAGATGTGAGG  
AGCACTCGGACAGGAGACCCCAATGTCTCAGTGCCTGTCTGGAGTTCAAGTGCAGTGGGATGCTCTATGA  
TCAGGACCGTGTGGACCGCACCTGGTGAAGGTATCCCCCAGGGCAGTGGCTGAGCCAGTGTGAACCCCA  
TGCTGCATGAGTACCTGGTCAACCACTTGGCACTGCAGTCAACAACGACACACAGTGAATACACCATGCTGGCA  
CCCTTGGACCCATGGGCGCAACACTATGGCATCTACATGTCACTGACCAGGACCTCGCACGGCCAAAGGAT  
CGCGCTCGGCGGCTGCTTTGATGGCACATCCGATGGCTCCTCAGAATCATGAAGCAATGTGGGAGTACGCC  
TCACCTTCAACTGTAGAGAGGCAAGTAGGCGCGCAGAGTGCTTCCAGTACCTCCAAGCACCAGCCGACCCG  
TCCCCTGCTGCAGGCACGTGCCAAGGAAGAGTGCCCTCGAGGAGGAGCAGCAGCGAGCGAGAGGGGTGGCCAGGC  
CAGGGTGGAGTGGTGGCCCTCTCTGAGATTTCTAGAGTTGCTCAACAGCCCTGATCAACTAAGTTTTGTGGT  
ACTTCAACCCTCTTCTGGCTTATTCTATGTGACAGCAATTGTAGACTGATGCACAACTGTCACTTGGTTTAA  
TTAAGCACTTCTGTTTTCTGTAATTTGCTTGTGTTGTTCTTCATGCCTTTACTTACTTTGTCCCATGCTACTGA  
TTGGCAGCTGGCCCAACATGGCACATAAAGGCCCTTTGTGAACCTGTTCTTTAAATGAACACAGAATAAT  
GGCACTGGTAAACTCTGCAGCTTCAACTGTACTTATTATTTGCCATTATGCAATATACTTCTCTCTT  
TTTGCATGGTTTTGGCCACCTCTGCAATAGTGATAATCTGATGCTGAAGATCAATAACCAATATAAAGCATAT  
TTCTTGGCTTGTCTCCACGAGCATAGGCAAGCCCTTGATCATAGTTCATACATATAAATGGTGGTGAATAAAG  
AAATAAAACCAATACTTTTACTTGAATGTAAATAACTTATTTATTTCTTTGCTAAATTTGAAATTCATGTG  
ACATTCAAAGTTAAGCTATTAATATAGGGTGATCATAGTTCTCTACCAAGTCTGGAAAGAACATCTCCTGGT  
ATCCACAATTCACCAAGGTGCTAATGTATTTGTACACTTCCCTTTGCATTCGCTTTTGTCTTGTGCTAGAAAC  
CCAGTATGCCCAAGGCGAGATGTCAATAAATGCATACTCTGTATTTTCCAAAAA



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**FIGURE 72**

MVGTKAWVFSFLVLEVTSVLGRQTM LTQSVRRVQPGKKNP SIFAKPADTLES PGEWTTWFNI  
DYPGGKG DYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ  
RPGQNC SNYTVRFLCPPGSLRRDTERIWSPWSPWSKCSAACGQTGVQTRTRICLAEMVSLCS  
EASEEGQH CMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGA AIYLLTK  
TPKLLTQTDS DGRFRI PGLCPDGKSILKITKVKFAPIVLTMPKTS LKAATIKAEFVRAETPY  
MVMNPETKARRAGQSVSLCCKATGKPRPD KYFWYHNDTLLDPSLYKHESKLVLRKLQHQAG  
EYFCKAQSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQ NATNSFY YDVGRCPV  
KTCAGQQDNGIRCRDAVQNC CGISKTEEREIQCSGYTLPTKVAKECSCQRCTETRSIVRGRV  
SAADNGEPMRFGHVYMGNSRVSM TGYKGTFTLHVPQDTERLVLT FVDRLQKFVNTTKVLPFN  
KKGSAVFHEIKMLRRKEPIT LEAMETNIIPLGEVVGEDPMAELEIPSR SFYRQNGEPYIGKV  
KASVTFLDPRNI STATAAQTDLNF INDEGDTFPLRTYGMFSVD FRDEVTSEPLNAGKVKVHL  
DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL  
DVPESRRCFVKVRAYR SERFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA  
CVP AFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQP YLNKLN YRRTDHEDPR  
VKKTA FQISMAKPRPNSAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTVPFN  
EDDPMSWTE DYLA WWP KPMEFRACYIKVKIVGPLEVNVRSRNMGGTHRRTVGKLYGIRDVRS  
TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTL VKVIPQGSRRASVNPMLHEYLVNHLPLAV  
NNDTSEYTM LAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTS DGSSRIMKSNVGVALT  
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGQRQGGVVASLRFPRVA  
QQPLIN

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**FIGURE 73**

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCTCAATATACCTGAATACGCAC  
AATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCATCTTCATTTAAAAAAAATACAGAG  
ACCTACCTACCCGTACGCATACATACATATGTGTATATATATGTAAACTAGACAAAGATCGCAGATCATAAAGC  
AAGCTCTGCTTTAGTTTTCCAAGAAGATTACAAAGAATTTAGAGATGTATTTGTCAAGATCCCTGTGCGATTATG  
CCCTTTGGGTTACGGTGTCTCAGTGATGCAGCCCTACCCTTTGGTTTGGGGACATTATGATTTGTGTAAGACT  
CAGATTTACACGGAAGAAGGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACATGACAAAATA  
TCTGAAAGTGAAACTCGATCCTCCGGATATTACCTGTGGAGACCCCTCTGAGACGTTCTGTGCAATGGGCAATC  
CCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGAGCTGGCACACCCCCCTGAGCTGATGTTTGATTTT  
GAAGGAAGACATCCCTCCACATTTTGGCAGTCTGCCACTTGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACAT  
CACTCTGTCTTGGAGCAAACCATTTAGCTAACAGACAACATAGTTATTACCTTTGAATCTGGGCGTCCAGACC  
AAATGATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAGACTGCTTA  
GATGCTTTTACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTCTTAGAAATCATTTGCACAGA  
AGAGTACTCAACAGGGTATACAACAAATAGCAAATAATCCACTTTGAAATCAAAGACAGGTTCCGCGCTTTTTG  
CTGGACCTCGCCTACGCAATATGGCTTCCCTCTACGGACAGCTGGATACAACCAAGAACTCAGAGATTTCTTT  
ACAGTCACAGACCTGAGGATAAGGCTGTTAAGACCAGCCGTTGGGGAAATATTTGTAGATGAGCTACACTTGGC  
ACGCTACTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGTAATCTCCATGCCACTGTATGTG  
TGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACTACAGGTCCAGACTGTGGGAAATGCAAGAAG  
AATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCCATCCCCAAAGGCACTGCAAATACCTGTATCCC  
CAGTATTTCCAGTATTGGTACGAATGTCTGCGACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACA  
ACAACGTGCGCTGCTGTGCCCGGCCGCATACAGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGC  
AGCTGCGGCTCCGACTCTGGCCAGGGCGCGCCCCCGCACGGCACCCCAAGCGCTGCTGCTGCTGACCACGCTGCT  
GGGAACCGCCAGCCCCCTGGTGTTCAGGTGTACCTCCAGCCACACCGGACGGGCTGTGCCGTGGGGAAGCA  
GACACAACCCAAACATTTGCTACTAACATAGGAAACACACATACAGACACCCCCACTCAGACAGTGTACAAA  
CTAAGAAGGCCTAACTGAACCTAAGCCATATTTATCACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTT  
TGACTCCAGAGGAGTTGGCAGCTGTTGATATTATCACTGCAATCACATTGCCAGCTGCAGAGCATATTGTGGA  
TTGGAAGGCTGCGACAGCCCCCAAACAGGAAAGACAAAAACAAACAAATCAACCGACCTAAAAACATTGGC  
TACTCTAGCGTGCTGCGCCCTAGTACGACTCCGCCCAGTGTGTGGACCAACCAATAGCATTCTTTGCTGTGAG  
GTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCTGCTTCCGTCCCTGAATCCCTTCCAAC  
CTGTGCTTTAGTGAACGTTGCTCTGTAACCCTCGTTGGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACA  
TGTGTAACAGCCCCCTCTAAAAGCGCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCGA  
GCACACACCCACTATACAAGAGTGGCTATAGGAAAAAAGAAAGTGTATCTATCCTTTTGTATTCAAATGAAGTT  
ATTTTCTTGAACCTACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGACAATCTGTTAAT  
GTATCTAATTGCAATCAGCAAAGACTGACATTTTATTTTGTCTCTTTTCTGTTCTGTTTTGTTCACTGTGCAGA  
GATTTCTCTGTAAGGGCAACGAACGTGCTGGCATCAAAGAATATCAGTTTACATATATAACAAGTGTAATAAGA  
TTCCACCAAAGGACATTCTAAATGTTTTCTTGTGCTTTAACTGGAAGATTTAAAGAATAAAAACTCCTGCA  
TAAACGATTTTCAAGGAATTTGTATTGCAATTTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTTCACTCACT  
TACTGATTTCTGTGTGGACTGAGTACATTGAGCTGACGAATTTAGTTCCCAGGAAGATGGATTGATGTTCACT  
AGCTTGGACAACCTTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTACAACAGCAAAAAAAAAAAAAA  
AAAAAA

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**FIGURE 74**

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK  
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK  
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMLEKSLDYGRTWQPYQYYATDCLDAF  
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD  
TTKKLRDFFTVDLRIRLLRPVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN  
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLPIPKGTANTCIPSISSIGTNVCDNELLH  
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS  
PLVF

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**FIGURE 75**

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTGCGCTAAGATTGCTGAGGAGGCGG  
CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCGGTCCGGGCGAGGTGTCCTCATGACTT  
CTCTTGTGGACCATGTCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC  
CCTCTCAGCCTCTACTGATTTTTTACCACACCCAAGATTTTTTGAATGGAGGAGACGGCTCA  
AGAGTTTAGCCTTGCGACTGGCCCAGTATCCAGGTGAGGTTCTGCAGAAGGTTGTGACTTT  
AGTATACATTTTTCTTCTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC  
AGCAGCCATGGCCTTCTGCTTCTGGAGACCCTGTGGTGGGAATTCACAGCTTCCTATGACA  
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTGAG  
AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGAAAAAAT  
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA  
ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA  
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT  
CATTCGAGGAGTTCACCTTGCGAAGCATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT  
TGGACCAAACCTCGTTGAGCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT  
CCGGGAGCAGTGATGTCAAACCTTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA  
AAAGGGCATGTCAGTGAAATCTGGGAATGGCTGGATTGCGAAACATCTGCCCATGTGTATTG  
ATGGCAGAGCTGTTGCCACAAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT  
TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCCTACATTTATATGATTCTGGGGTT  
GCTTCAGAAGTGTTATTTTCATGAATCATTTCATATGATTGATCCCCCAGGATTCTATTTTGT  
TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAACCAT  
TTACTTTACATATTCGTTTTCAATACTTGCTGTTTCATGTTACACAAGCTTCTTACGGTTTTTC  
TTGTAACAATAAATATTTTGAGTAAATAATGGGTACATTTTAACAACTCAGTAGTACAACC  
TAACTTGTATAAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAAATG  
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTTTATTAAAAAATAAAAAAAAAAAAAA  
AAAAG

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**FIGURE 76**

MSVIAFFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFS IHF  
SSF GDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQKVKW  
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLED TDVANGVMNGHTPMHLEPAPNFRMEPVTA  
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

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**FIGURE 77**

TGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT  
AGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTGAGAAAGTGAAGTGGCATT  
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAGGAGGAGCTCAAG  
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

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**FIGURE 78**

CTCAGCGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA  
CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAACGAGGCGGGTGGTG  
CCTGCCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT  
TCTGTGCGAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT  
CCTCCCCGCTCGTCCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTA  
TGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCACGAGAGGATCCGC  
GAGTGTATTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGAC  
CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA  
TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCTGCTCCTGCC  
TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACACTACATCCAGTGGCT  
CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTCTCTTCCCCAACCTGTCCCTCA  
TCTTCCCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG  
GGTGTCTGGGCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT  
AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT  
ATGACTTTTGGGAGTACTATCTCCCCTACCTCTACTCATGCATCTCCTTCCTTGGGGTTCTG  
CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT  
AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG  
CAGCCCTGACCCGCAGGATCTGTAATCCTACTTCCTGCTGGCTGCCTTTAGACATGGAGCTG  
CTACACAGACAGGTCTGGCTCTGCAGACACAGAGGGTCTGCTGGAGAAGAGGCGGAAGGC  
TTCAGCCTGGCAACGGAACCTGGGCTACCCCCTGGCTATGCTGTGCTTGTGCTGCTGACGG  
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG  
CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG  
TGCCGTCATTCAGGTTGTACTCATCTTTTACCTAATGGTGTCTCAGTTGTGGGCTTCTATA  
GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT  
GGGAAGTGTGTCTGTCTCCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCTGGG  
GCTCACTCGCTTTGACCTGCTGGGTGACTTTGGACGCTTCAACTGGCTGGGCAATTTCTACA  
TTGTGTTCTCTACAACGCAGCCTTTGCAGGCCTCACCACACTCTGTCTGGTGAAGACCTTC  
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT  
CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAGTGAACCTCCAGCTGGGGGTGGGA  
AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG  
ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT  
GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT  
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCTGATCCCAAATCTGTTTACACATCA  
ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT  
AGGGTGGGGTAGGGGCAGGGAAGGACTGGGCCAGGGCAGGCTCGGGAGATAGATTGTCTCC  
CTTGCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG  
AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA  
AAAAAA

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**FIGURE 79**

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDDEDATVNK  
IALELCTFTLAIALGAVLLLPSIISNEVLLSLPRNYIQWLNGSLIHGLWNLVFLFPNLSL  
IFLMPFAYFFTESEGFAGSRKGVLRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL  
YDFWEYYPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE  
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRVLLKRRKASAWQRNLGYPLAMLCLLVLT  
GLSVLIVAIHILELLIDEAAMPQGTSLGQVSFSKLGSGFQVLIQVVLIFYLMVSSVVGFY  
SSPLFRSLRPRWHDAMTQIIGNCVCLLVSSALPVFSRTLGLTRFDLLGDFGRFNWLGIFY  
IVFLYNAAFAGLTTLCLVKTFATAAVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ



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**FIGURE 80**

GGCTGCCGAGGGAAGGCCCTTGGGTTGGTCTTGGTTGCTTGGCGGCGGCGGNTTCNTCCCC  
GCTCGTCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC  
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA  
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC  
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG

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**FIGURE 81**

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTTAAAACGAGGCGGTGGTGC  
CTGCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTTTC  
TGTCGCAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGTGCTTGGCGGCGGCGGCTTCCT  
CCCCGTTGTCNTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA  
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT  
GTATTATATCAACACTTCTGTTTGCAACACTGTACATCNTCTGCCACATCTTCCTGACCCGC  
TTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGATTGC  
GCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCTCCTGCCCTTCT  
CCATCATCAGCAATGAGGTGCTGCACTCCC

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**FIGURE 82**

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTGACTGTAAGATCAAGTCCAAACCTGTTTT  
GGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTCCATGCTGCTGT  
GGGTGATATTACTGGTCCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGGCCCAT  
ATTTTCCTCCAGCCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCCTCACTTGCAA  
GGGATTTTCGCTTCTACTCACCACAGAAAACAAATGGTACCATCGGTACCTTGGGAAAGAAA  
TACTAAGAGAAACCCAGACAATATCCTTGAGGTTTCAGGAATCTGGAGAGTACAGATGCCAG  
GCCCAGGGCTCCCCCTCTCAGTAGCCCTGTGCACTTGGATTTTTCTTCAGAGATGGGATTTCC  
TCATGCTGCCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTGCTCACCCTAGGCCTCTC  
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTTCTGTGTTTGAAGGAGAC  
TCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTGAATAATACTATTTACAAGAA  
TGATAATGTCCTGGCATTCTTAATAAAAGAACTGACTTCCAAAAAAAAAAAAAAAAAAAAA  
AAA

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**FIGURE 83**

MLLWVILLVLAPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL  
GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLDFSSEMGFPHAAQANVELLGSSDLLT

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**FIGURE 84**

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCCGCGCCCCCCCCGGTGT  
GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG  
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACCATGGCTCCGCAGAACCTGAGCACCTTTT  
GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG  
GGGTGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAACTAGCCCTGCA  
GCTTCATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCAGGATCTGGGTG  
CTGCTTATGAGGTTCTGTGAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA  
GGATTAAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTCACACTTCTTTGGGGATTT  
TGTTTTTCATGTTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA  
TTATTGTAGATCTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT  
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGAT  
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT  
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG  
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG  
AGATTTACGGTTCCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT  
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT  
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT  
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA  
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA  
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATATTGAGAGTG  
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT  
TTGTGTGTGTTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTTATCTAATGA  
TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTGGGAAAAGAATGACC  
AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGT  
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA  
GTTGTTAGCAATTTCAATCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTG  
TTATTTTAA

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**FIGURE 85**

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQ  
AQEKFQDLGAAYEVLSDSEKRRKQYDTYGEGLKDGHQSSHGDIFSHFFGDFGFMFGGTPRQQ  
DRNI PRGSDIIVDLEVTLEEYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ  
MTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGMETPFIGE GEPHVDGEPGD LRFRIKVVKH  
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDG HKVHISRDKITRPGAKLWKKGEGLPNFD  
NNNIKGS LIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

**Important features:****Signal peptide:**

amino acids 1-22

**Cell attachment sequence.**

amino acids 254-257

**Nt-dnaJ domain signature.**

amino acids 67-87

**Homologous region to Nt-dnaJ domain proteins.**

amino acids 26-58

**N-glycosylation site.**

amino acids 5-9, 261-265

**Tyrosine kinase phosphorylation site.**

amino acids 253-260

**N-myristoylation site.**

amino acids 18-24, 31-37, 93-99, 215-221

**Amidation site.**

amino acids 164-168

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**FIGURE 86**

TGGGACCAGGGAACCCCGGGCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA  
GCGGCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT  
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG  
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAGGATATTAAAAAGG  
CCTATAGGAACTAGCCCTGCAGNTTATCCCGACCGGAACCCTGATGATCCACAAGCCCAG  
GAGAAATTCAGGATTTGGGTGCTGCTTATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA  
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT  
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA  
AATATTCCAAGAG

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**FIGURE 87**

GGCACGAGGCGGCGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT  
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA  
GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGCATGG  
AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGCAGCC  
TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGGCCGCGAGACCTGCTGCAGCGCTATGATTC  
TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC  
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC  
GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACACTCTGAC  
AGAGAAGCTTGTTGCCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA  
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG  
TACCCTCCGTTGGACCCCAAACCTCCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGTGAC  
TCACCTGGTGCTGGTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC  
AGTCTCTGTGCGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG  
CCAGATAAAGGCCTCCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATTTAGTGCCT  
ACAGGCCAGCAGCTAGCCATGAAGGCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT  
CTACTTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGTGCATAG  
TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACCTGTGGCTGGTGAGT  
GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA  
CTGGTGGACTGTCAGCTTTATTTAGCTCACCTAGTGTTTTCAAGAAAATTGAGCCACCGTCT  
AAGAAATCAAGAGGTTTACATTAAATAGAAATTTCTGGCCTCTCTCGATCGGTCAGAATG  
TGTGGCAATTCTGATCTGCATTTTTCAGAAGAGGACAATCAATTGAACTAAGTAGGGGTTTC  
TTCTTTTGGCAAGACTTGTA CTCTCACCTGGCCTGTTTCATTTATTTGTATTATCTGCCT  
GGTCCCTGAGGCGTCTGGGTCTCTCCTCTCCCTTGCAAGTTTGGGTTTGAAGCTGAGGAACT  
ACAAAGTTGATGATTTCTTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG  
GATAGTAAATTTATACTTATGTTTCCCTCAAAAAAAAAAAAAA



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**FIGURE 88**

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSESEL  
ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKMKTSAS  
VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLSVSHLVLVTRNACHLTGGLDWI  
DQSLSAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

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**FIGURE 89**

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTCCGAGGTGCTTTCGCCGCTGTCC  
CCACCACTGCAGCCATGATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA  
TTTGGAGTGTTTTTCCTGTTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT  
TGGAATGTTTTATTTGTAGCCGGCTTGGCTTTTGTAAATTGGTTTAGAAAGAACATTCAGAT  
TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTC  
CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTTCTCTTGTTTCAG  
GGGCTTCTTTCCTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT  
TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTATTAACAACA  
AGTGAATTTGAAGACTCATTTAAAATATTGTGTTATTTATAAAGTCATTTGAAGAATATTCA  
GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG  
CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA  
ACTAAGAAGAAGTCAGCAAGCAAAGTGAAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA  
ACTCTTGAAGGCTATTTGTGTTGTTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA  
CTGTGGTGCCTGTTTCTTTTCTTTTTATTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT  
TTTTAGAAGTGTCCACTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA  
TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG  
ATGTATGGATTACTTTTTTTTTGNGCNCAGGGCC

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## **FIGURE 90**

MISLTDTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK  
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFI RRVPVLGSLLNLPGI  
RSFVDKVGESNNMV

**Important features:**

**Transmembrane domains:**

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

**N-myristoylation sites.**

amino acids 11-16, 51-56 and 116-121

**Aminoacyl-transfer RNA synthetases class-II protein.**

amino acids 49-59

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**FIGURE 91**

GAAGACGTGGCGGCTCTCGCCTGGGCTGTTTCCCGGCTTCATTTCTCCCGACTCAGCTTCCC  
ACCNTGGGCTTTCCGAGGTGCTTTTCGCCGCTGTCCCCACCACTGCAGCCATGATCTCCTTAA  
CGGACACGCAGAAAATTGGAATGGGATTAACCGGATTTGGAGTGTTTTTCCTGTTCTTTGGA  
ATGATTCTCTTTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTTATTGTAGCCGGCTT  
GGCTTTTGTAATTGGTTTAGAAAGAACATTCAGATTCTTCTTCCAAAACATAAAATGAAAG  
CTACAGGTTTTTTTCTGGGTGGTGTATTTGTAGTCCTTATTGGTTGGCCTTTGATAGGCATG  
ATCTTCGAAATTTATGGATTTTTTCTCTTGTTT

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**FIGURE 92**

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA  
GGCTGCCAGGAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCTTCTGGAAATCTTTGA  
CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC  
TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC  
ATCAACACCATTTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA  
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT  
CGGGCACGGAATGCACCATCTTCACGGACCCGCGCGCCTACCTCAAGTATGGGAAGGAAAAT  
GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA  
ACGCTTTGGGCTGTTAGGGGGCTCCAAGGTCCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA  
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTTCGCGCAAGTGGGAGCAGGAT  
CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCTCT  
GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC  
GGGCCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC  
ACCGTGAGGAGCTTGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTTCAGAAA  
TAATGAAAATCCAACACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATG  
TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC  
AAGCTCTACCAGGAGAAGGATGCCTTTTCAGGAGGAGTACTACAGGACGGGCACCTTCCCAGA  
GACGCCCATGGTGCCCCCGGCGGCCCTGGACCCTCGTGAAGTGGCTGTTTTGGGCCTCGC  
TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG  
CTGGCCAGCTTCATCCTCGTCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGT  
GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAAGCAGAACTGAATGACT  
GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT  
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCCTGCTGGGCACGGCGGAAGTCACGA  
CCTCTCCAGCCAGGGAGTCTGGTCTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTT  
TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTGTGCGAGTGTGTGTGAGAATGGC  
TGTGTGGTGAGTGTGAACCTTTGTTCTGTGATCATAGAAAGGGTATTTTAGGCTGCAGGGGAG  
GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCCTTTTCATCCTTTGGTGCTGAGTTTTCTGT  
AACCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC  
CAAGAAAAAAAATTAAGTGCTTTTCTGGGTCAAAAAAAAAA

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**FIGURE 93**

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLV  
MLLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHNKFEIDFLCGWSLSERFGLLGSKVLAKK  
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQHLDYPEKYFFLIHCEGTRFTEKKHE  
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVNLGKK  
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWTLVN  
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS  
KQKLND

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**FIGURE 94**

CTGAGGCGGCGGTAGCATGGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG  
GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA  
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA  
TACAATTGACATTCAGAAATATATTCCATGCTATCAGCTTTTTAGCTTTTATAATTCTTCAG  
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT  
TGGTACAAATTCCGTCGTCATTCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAA  
AACTTGCAGGAGCATTTTTTCAAACCAAGACCTTGTTTTTCTGCTATTAACACCAAGTATAA  
TAACAGAAAGCTGCTCTACTCATCGACTGGAACATTCCCTTATATAAACCTCAAAAAGGACTT  
TTTCACAGGGTACCTTTAGTGTTGCCAATCTGGGCATGTCTGAACAAGTGGTTATAAAAC  
TGTATCAGGTTCCGTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT  
TTTTTGAAGAAGATGGATCCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA  
CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT  
AGTAAAGGATGTAAACAGATTAAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG  
CAGCAAGAGAGAAGAACATCCAAAAAGACCCTCAGGAGAACATTTTTCTTTGTCAGGCATTA  
CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTTCATGTGTTATGTCTTTAAAAAATAGACA  
TGTTTCTAAAGTAGCTGTAAC TACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA  
TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCAT  
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAGAGATCTCGGTTGTTAGATACACAAGA  
CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAATGAGCAGCC  
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA  
TTTTTGATCCTTTTAACTTACAAGGAGATTTTTTTATTTGGCTGATGGGTAAAGCCAAACAT  
TTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTTAC  
CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAAC  
ATCAGATGCTTTTTATTTCCAAACCTTTTTTTTACCTTTCACTAAGTTGTTGAGGGGAAGGCT  
TACACAGACACATTCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA  
TCCCAGCACTTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC  
TGGGCAACGTATTGAGACCATGTCTATTAAAAAATAAAATGGAAAAGCAAGAATAGCCTTAT  
TTTCAAAATATGGAAAGAAATTTATATGAAAATTTATCTGAGTCATTAAAATTCTCCTTAAG  
TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA  
ATAAATTTGCAAAACATCATCTAAATTTAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 95**

MEGESTSAVLSGFVLGALAFQHLNTSDTEGFLLG EVKGEAKNSITDSQMDDVEVVYTI DIQ  
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH  
FSNQDLVFLLLTPSIITESCSTHRLEHS LYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC  
MSTGFSRAVQTHSSKFFEE DGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN  
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS  
CNYNHHLDVVDNL TLMVEHTDIPEASPASTPQIIKHKALDLDDRWQFKRSRLLD TQDKRSKA  
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSP TF



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**FIGURE 96**

GGCACAGCCGCGCGGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCAGCGCAGGGCAGC  
CCAAGCAGCGCGCAGCGAACGCCCGCCGCCACACCCTCTGCGGTCCCCGCGGCGCCTGCCACCCTTCCCT  
CCTTCCCCGCGTCCCCGCTCGCCGGCCAGTCAGCTTGCCGGGTTGCTGCCCCGCGAAACCCCGAGGTCACCA  
GCCCCGCGCTCTGCTTCCCTGGGCGCGCGCCGCTCCACGCCCTCCTTCTCCCCTGGCCCGCGCCTGGCACC  
GGGGACCGTTGCCTGACGCGAGGCCCAGCTCTACTTTTCGCCCCGCTCTCCTCCGCTGCTCGCCTCTTCCAC  
CAACTCCAACCTCCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCCCGCTGCCGTAG  
CGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCGGCCCGCACCATGGCACGGTTCCGCTTGCC  
CGCGCTTCTCTGCACCCTGGCAGTGCTCAGCGCCGCGTGTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGG  
AAGTGCAGCGTCTTTACGTGTCCAAAGGCTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCAT  
TTGAAGATCTGTCCCCAGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAGTAAAGA  
TGATTTCAAAGTGTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTACGTTACAAGAAGTTTG  
ATGAATTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGTTTGTGAAGACATATGGCCAT  
TTATACATGCAAAATTCTGAGCTATTTAAAGATCTCTTCGTAGAGTTGAAACGTTACTACGTGGTGGGAAATGT  
GAACCTGGAAGAAATGCTAAATGACTTCTGGGCTCGCCTCCTGGAGCGGATGTTCCGCTGGTGAATCCCAGT  
ACCCTTTACAGATGAGTATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCT  
CGCAAAATTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCGTAAGCTTTTCAAGGCTTAGCGGTTGCGGG  
AGATGTCGTGAGCAAGGTCTCCGTGGTAAACCCACAGCCAGTGTAACCATGCCCTGTTGAAGATGATCTACT  
GCTCCCACTGCCGGGCTCTCGTGAAGCCATGTTACAACCTACTGCTCAAACATCATGAGAGGCTGTTTG  
GCCAACCAAGGGGATCTCGATTTTGAATGGAACAATTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGA  
GGGTCCTTTCAACATTGAATCGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGG  
ATAATAGTGTTCAAGTGCTCAGAAGGTTTTCAGGGATGTGGACCCCCCAAGCCCTCCAGCTGGACGAATT  
TCTCGTTCCATCTCTGAAAGTGCCTTCAGTGCTCGCTTCAGACCACATCACCCCGAGGAACGCCCAACACAGC  
AGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAACTGAAACAGGCCAAGAAATCTGGTCCT  
CCCTTCCGAGCAACGTTTGCAACGATGAGAGGATGGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGG  
AAAGGCAAAAGCAGGTACCTGTTTGCAGTGACAGGAAATGGATTAGCCAACAGGGCAACAACCCAGAGGTCCA  
GGTTGACACCAGCAAACCAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGATGA  
AGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAGAAGGAAGTGGAGT  
GGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAATGCCACTGACCATGCTGGGAAGAGTGCCAATGA  
GAAAGCCGACAGTGCTGGTGTCCGTCTGGGGCACAGGCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGG  
TTATGCAGAGAGAGTGGAGATTAATTCTCAAACCTCTGAGAAAAAGTGTTTCATCAAAAAGTTAAAGGCCACAGTT  
ATCACTTTTCTACCATCCTAGTGACTTTGCTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC  
CACTGGTTTAAAGAAGTGCTGACTTTGTTTTCTCATTAGTTTTGGGAGGAAAAGGACTGTGCATTGAGTTGGT  
TCCTGCTCCCCCAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAACTATAGTTAGTTGTGCATTTGTGA  
TTTTATCACTCTATTATTTGTTTGTATGTTTTTTCTCATTTCGTTTGTGGGTTTTTTTTTCCAACGTGATCT  
CGCCTTGTCTTACAAGCAAACAGGGTCCCTTCTTGGCAGTAACATGTACGTATTTCTGAAATATTAAATA  
GCTGTACAGAAGCAGGTTTTATTTATCATGTTATCTTATTTAAAGAAAAAGCCAAAAAGC

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**FIGURE 97**

MARFGLPALLCTLAVLSAALLAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ  
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMF  
VKTYGHLYMQNSSELFKDLFVELKRYVVGNVNLEEMLNDFWARLLERMFRLVNSQYHFTDEY  
LECVSKYTEQLKPFQDVPRKLLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL  
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLD FEWNNFIDAMLMVAERLEGPFNIES  
VMDPIDVKISDAIMNMQDNSVQVSQKVFQCGPPKPLPAGRISRISSESARFRPHHPEE  
RPTTAAGTSLDRLVTDVKEKLKQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYL  
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFDISDESSGE  
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

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**FIGURE 98**

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCT  
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAA  
GCAACTTACAGCTGCACCGACAGTTGCGATGAAGTTCTAATCTCTTCCCTCCTCCTGTTGC  
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCAC  
AGGGACCGAGGCCAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAA  
AGATTGGTTCCTGAGAGCCCCGAGAAGAAAATTCATGACAGTGTCTGGGCTGCCAAAGAAGC  
AGTGCCCCTGTGATCATTTCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCCACAGA  
AAGCCAAACAAGCATTCAGAGCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTT  
TGCTCTGCCTTTGTAGGAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA  
GACAGTGAGCACACCTACCAGACACTCTTCTTCTCCACCTCACTCTCCCACTGTACCCACC  
CCTAAATCATTCCAGTGCTCTCAAAAAGCATGTTTTTCAAGATCATTTTGTTTGTTGCTCTC  
TCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCCTTACCCAGGCTTAGGCTT  
AATTACCTGAAAGATTCCAGGAACTGTAGCTTCCCTAGCTAGTGTCAATTAACCTTAAATGC  
AATCAGGAAAGTAGCAAACAGAAGTCAATAAATATTTTTAAATGTCAAAAAAAAAAAAAAAAAA

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**FIGURE 99**

MKVLISLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR  
KFMTVSGLPKKQCPCDHFKGNVKKTRHQRRHRKPNKHSRACQQFLKQCQLRSFALPL

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**FIGURE 100**

**AATG**GCTGTCTTAGTACTTCGCCTGACAGTTGTCCTGGGACTGCTTGTCTTATTCCTGACCT  
GCTATGCAGACGACAAACCAGACAAGCCAGACGACAAGCCAGACGACTCGGGCAAAGACCCA  
AAGCCAGACTTCCCCAAATTCCTAAGCCTCCTGGGCACAGAGATCATTGAGAATGCAGTCGA  
GTTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTTATGGAATTTGATGATAATGAAGGAA  
AACATTCATCAAAG**TGA**CATCCTCAGGACACACCCATGTGGCTCCTGGACAATCCAAGAGCA  
GCCAAATCCTGCTTTTCCAGTTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTCAAAGCAAC  
TCCCAACGAGTTCTCAGGATTCAGGCTCTGGCTTCAACCAAACAGAACTCATTTTGAACACC  
CTGACTGCATTTTTGCTTTTAGAAAGTTAGAATAAATATGGCGCTTTGGGATCACATAGTTG  
ATGGAGAGGAAA

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**FIGURE 101**

MAVLVLRRLTVVLGLLVLFLTCYADDKPKDKPDDSGKDPKPDFPKFLSLLGTEIIENAVE  
FILRSMRSTGFMEFDDNEGKHSSK

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**FIGURE 102**

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT  
CAGAGCTGGTCTGCCATGGACATCCTGGTCCCCTCCTGCAGCTGCTGGTGCTGCTTCTTAC  
CCTGCCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCCTGTGCAAAAGCTACTTCC  
CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG  
CTCTTCAGCCAGATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG  
CTGCGGAACCGGAGCCAACTTTCAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC  
CAAATCCCCACTTTGAGAAGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT  
GAGCGGTTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT  
GGTGGTCTGCACTCTGGTGTCTGTGCTCTGTGCAGAGCCCAAGGAAGTCTGCAGGAGGTCC  
GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA  
AGCTGGGCCTTCATGTGGCAGCAAGTTTTCTGAGCCCACCTGGAAACACATTGGGGATGGCTG  
CTGCCTCACCAGAGAGACCTGGAAGGATCTTGAGAACGCCAGTTCTCCGAAATCCAAATGG  
AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC  
AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA  
AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCTTAGCAGAATGAGAGAAGACATT  
CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC  
CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC  
TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC  
CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT  
CTCTAGGAACCTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCCTGACCCTCT  
CTCCCCACTACCACCTTCTTCCCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT  
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTTCTCAAATATTTTTTAATAAATAGACGA  
AACCACG

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**FIGURE 103**

MDILVPLLQLLVLLLTPLPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQL  
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCCLDPNPHFEKFLTKSMAENRHLQYERFVV  
APGEDMRQLADGSMDVVVCTLVLCSVQSPRKVLQEVRRLRPGGVLFFWEHVAEPYGSWAFM  
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPGVPHIMGKAVKQSFP  
SSKALICSFPSLQLEQATHQPIYLPLRGT



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**FIGURE 104**

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGGAAGTTGCCTCATCGCAGG  
CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA  
ACTAATATTTATATGACAGAAGAAAAAGATGTCATTCCGTAAAGTAAACATCATCATCTTGG  
TCCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG  
TTAAGGAATGAGGTTACAGATTCAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAA  
TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATCTG  
AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTTCAGCACAACTCGCTCCAAT  
GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAG  
TGATTCCCTGAAAAGCATCAGATACAAAATTGTCAATTTTGACCTAAACTTTTGGAAGGAA  
AAGTAAAGGAGGATCCTGACCAGGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC  
TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGTAATTGTGCA  
AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG  
AAGATTGTGATTTCAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC  
ATTGGCTATCTTGACTATAAAAAGGAAAGAATTTCGTAAGCTTTCCATGAAAGCCAGCACTTG  
CTCATTTAATCCTGGAGTTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA  
ACCAACTGGAAAAATGGATGAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCCTGGCT  
GGTAGCATCACAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC  
TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTA  
AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT  
ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTCACCTAATCCGAAG  
ATATACCGAGATCTCAAACATAAAGTGAACAGAAATTTGAACTGTAAGCAAGCATTCTCAG  
GAAGTCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA  
GCAAGCCATGGAAAAAGATGTGTCAGCTAGGTAAAGATGACAACTGCCCTGTCTGGCAGTC  
AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTTTTCTT  
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTTCAGCTAGCTGGTACAGA  
TAATTCAAACCTGCTGTTGGTTTTAATTTTGTAACCTGTGGCCTGATCTGTAAATAAACTT  
ACATTTTTC

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**FIGURE 105**

MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLLRNEVTDSGIVGPQPIDFVPNALRHAVDGR  
QEEIPVVIAASEDRLGGAIAAINSIQHNTRSNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK  
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT  
ALKPGHAAAFSEDCDSASTKV VIRGAGNQYNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA  
NLTEWKRQNITNQLEKWMKLNVEEGLYSRTL AGSITTPPLLIVFYQQHSTIDPMWNVRHLGS  
SAGKRYSPQFVKA AKLLHWNGHLKPWGRTASYTDVWEKWIIPDPTGKFNLIRRYTEISNIK

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**FIGURE 106**

TGGTTTTTGCCCCATAAATTCCTCAGCTTGAGCAGTTTGTTAAGGAATGAGGTTACAGATT  
CAGGAATTNTAGGNCCTCAACCTNTAGANTTTGTCCCAAATGTTCTCCGACATGCAGTAGAT  
GGGAGACAAGAGGAGATTCCCTGTGGTCATCGCTGCATNTGAAGACAGGCTTGGGGGGGCCAT  
TGCAGCTATAAACAGCATTTCAGCACAACTCGNTCCAATGTGATTTTCTACATTGTTACTC  
TCAACAATACAGCAGACCATNTCCGGTCCTGGNTCAACAGTGATTCCCTGAAAAGCATCAGA  
TACAAAATTGTCAATTTTGACCCTAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCA  
GGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGTTCCCAGCG  
CAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTAC  
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTAC  
TAAAGTTGTCATCCGTGGAGCAGGAAA

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**FIGURE 107**

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCTGGGCGTAGTGGGGCTGCGCGGCTGCCACG  
GAGCTAGAGGGCAAGTGTGCTCGGCCAGCGTGCAGGGAACGCGGGCGGCCAGACAACGGGC  
TGGGCTCCGGGGCCTGCGGCGCGGGCGCTGAGCTGGCAGGGCGGGTCGGGGCGCGGGCTGCA  
TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT  
TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGGAGCGTCACATCACT  
TTCCGATCACTTCAAAGTGGTTAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT  
CCGTAAAGTAAACATCATCATCTTGGTCCTGGGCTGTTGCTCTCTTCTTACTGGTTTTGCAC  
CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTCAGGAATTGTAG  
GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA  
GGAGATTCCCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA  
ACAGCATTCAGCACAACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA  
GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG  
TCAATTTTGACCCTAACTTTTGGAAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGGAATCC  
ATGAAACCTTTAACTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCAGCGCAAAGAAGG  
CCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA  
CTGAAGCCAGGACATGCAGCTGCATTTTTCAGAAGATTGTGATTTCAGCCTCTACTAAAGTTGT  
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA  
TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTGCAAAC  
CTGACGGAATGGAAACGACAGAATATACTAACCAACTGGAAAAATGGATGAACTCAATGT  
AGAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAAACACCTCCTCTGCTTATCG  
TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT  
GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA  
TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA  
GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA  
CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG  
TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG  
GTAAAGATGACAACTGCCCTGTCTGGCAGTCAGCTTCCCAGACAGACTATAGACTATAAAT  
ATGTCTCCATCTGCCTTACCAAGTGTTTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA  
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAACTGCTGTTGGTTTTAATTTT  
GTAACCTGTGGCCTGATCTGTAAATAAACTTACATTTTCAATAGGTAAAAA  
AAAAA

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**FIGURE 108**

CTGCAGGTAGACATCTCCACTGCCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT  
GAAGGCCGGCCATACCAGAGTCCTGCCTCGGCATGGGCCTCACCATTGAGGCAGCTCCACTG  
TCTGTGCTGGTCTGAGGGTGCTGCCTGTCATGGGGGCAGCCATCTCCCAGGGGGCCCTCATC  
GCCATCGTCTGCAACGGTCTCGTGGGCTTCTTGCTGCTGCTGCTCTGGGTCATCCTCTGCTG  
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTCTGAATCCAGTCCCAACTCCAGCCC  
TGGCCCCTGTCCTGAGAAGGCCCCACCACCCCAGAAGCCCAGCCATGAAGGCAGCTACCTGC  
TGCAGCCCTGAAGGCCCTGGCCTAGCCTGGAGCCCAGGACCTTAAGTCCACCTCACCTAGAG  
CCTGGAATTAGGATCCCAGAGTTCAGCCAGCCTGGGGTCCAGAACTCAAGAGTCCGCCTGCT  
TGGAGCTGGACCCAGCGGCCCAGAGTCTAGCCAGCTTGGCTCCAATAGGAGCTCAGTGGCCC  
TAAGGAGATGGGCCTGGGGTGGGGGCTTATGAGTTGGTGCTAGAGCCAGGGCCATCTGGACT  
ATGCTCCATCCCAAGGGCCAAGGGTCAGGGGCCGGGTCCACTCTTCCCTAGGCTGAGCACC  
TCTAGGCCCTCTAGGTGGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG  
GCTGGGCCCTCCCCCTGGTCCTCCAGTGTTTGCTGGATAATAAATGGAACCTATGGCTCTAA  
AAAAAAAAAAAAAAAAA

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**FIGURE 109**

MGAAISQGALIAIVCNGLVGFLLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRPHH  
PRSPAMKAATCCSPEGPWPSLEPRT

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**FIGURE 110**

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA  
GTTCCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA  
CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGA  
TCATGTCGGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC  
ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTCAATTGGTTAT  
TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC  
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCGTGCTGGGGTTTGCTATCGTA  
TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT  
GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC  
AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCTCTGGGTGGCTGTGCTGCTG  
AGCCTGGGAAGTGCAGGAGCTGCCAGGTTATGGAAGGCGGCCAAGTGGAATATAAGCCCCT  
TTCGGGCATTTCGGTACATGTGGTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA  
TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT  
AAAAATGATCCTCCTGATCATCCCATCCTTTCGTCTCTCTCCATTCTCTTCTTCTACCATCA  
AGGAACCGTTGTGAAAGGGTCATTTTTAATCTCTGTGGTGAGGATTCGAGAAATCATTGTCA  
TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTGCAATTGTCCAGGTACCTGTTCCGA  
TGCTGCTACTGCTGTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA  
TACTACAAGTCTATTAATGGGACAGATTTCTGTACATCAGCAAAAGATGCATTCAAATCT  
TGTTCAAGAACTCAAGTCACTTTACATCTATTAAGTCTTTGGAGACTTCATAATTTTTCTA  
GGAAAGGTGTTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG  
GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTGCCTACTTAGTAGCCC  
ATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTGAT  
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT  
CGTAAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA  
ATGAGGAGGGAACAGAACTCCAGGCCATTGTGAGATAGATACCCATTTAGGTATCTGTACCT  
GGAAACATTTCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT  
AGTGAATTTTTTTTTTAAAGACCTAATAAACCTATTCTTCCTCAAAA

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**FIGURE 111**

MSGRDTILGLCILALALSLAMMFTFRFITLLVHIFISLVILGLLFVCGVLWWLYYDYTNDL  
SIELDTERENMKCVLGFAIVSTGITAVLLVLI FVLRKRIKLTVELFQITNKAISSAPFLLFQ  
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI  
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM  
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL  
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH  
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN  
EEGTELQAIVR





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**FIGURE 113**

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC  
PAGCQDPKYHVGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL  
SLPRWRESFIVLESKPKKGVTPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMQ  
LLAVTVAVATPTTLPRPSPSAASTTSIPRPQSVGHRSEQEMDLWSTATYTSSQNRPRADPGIQ  
RQDPSGAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR  
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATFNLKTHTNLSDLDKTAIEKITQRGGLSNV  
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE  
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLPVLRVCDTDRACSKTCLNSADI  
GFVIDGSSSVGTGNFRTVLQFVTNLTKFEISDTDRIGAVQYTYEQRLFEFGFDKYSSKPD  
LNAIKRVGYWGGTSTGAAINFALEQLFKKSKPNKRKLMILITDGRSYDDVRI PAMAAHLKG  
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFDNLHQYVPRI IQNICTEFNSQPRN

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**FIGURE 114**

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA  
TGCCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT  
GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT  
TGATGCACTGGACACCTTGCTGATTTTGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG  
TGCTCCAGGACAGCGTGGACTTTGATATTGATGTGAACGCCTCTGTGTTTGAACAAACATT  
CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA  
GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAATGGCTGAGGAGGCGGCCCGAAAACCTCC  
TCCCAGCCTTTTCAACCCCCACTGGCATGCCATATGGAACAGTGAACCTTACTTCATGGCGTG  
AACCCAGGAGAGACCCCTGTACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC  
CACCTTGAGCAGCCTCACTGGTGACCCGGTGTTTGAAGATGTGGCCAGAGTGGCTTTGATGC  
GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC  
AAGTGGGTGGCCCAGGACGCAGGCATCGGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT  
GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCTAGAGTATAACAAAG  
CCATCCGGAACCTACACCCGCTTCGATGACTGGTACCTGTGGGTTTCAAGTGTACAAGGGGACT  
GTGTCCATGCCAGTCTTCCAGTCCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG  
AGACATTGACAATGCCATGAGGACCTTCCTCACTACTACACTGTATGGAAGCAGTTTGGGG  
GGCTCCCGGAATTCTACAACATTCTCAGGGATACACAGTGGAGAAGCGAGAGGGGCTACCCA  
CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT  
CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGC GGAT  
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG  
GCCGAGACTGTGAAAATACCTCTACCTCCTGTTTGACCCAACCACTTCATCCACAACAATGG  
GTCCACCTTCGACGCGGTGATCACCCCTATGGGGAGTGCATCCTGGGGGCTGGGGGGTACA  
TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG  
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC  
GAAATTTCAGAAAAACACTGTTAGTTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC  
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCCA  
CTTCTCAGCTGCCCCAGTCAGCCCTTACCTCCAAGTTGGCATTACTGGGACAGGTTTTCTT  
AGACTCCTCATAACCACTGGATAATTTTTTTATTTTTATTTTTTTGAGGCTAAACTATAATA  
AATTGCTTTTGGCTATCATAAAA

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**FIGURE 115**

MPFRLLIPLGLLCALLPQHGGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE  
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLLSKKAGVEVEAGWPCSGPLLRMAEEAARKL  
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM  
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK  
AIRNYTRFDDWYLWVQMYKGTVSMPVFQSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG  
GLPEFYNIPOGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG  
FATIKDLRDHKL DNRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY  
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT  
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS

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**FIGURE 116**

AAAGTTACATTTTCTCTGGA ACTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG  
GGCAGAAAGGAGGGTGCTTCGGAGCCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA  
ATTCAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT  
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAA ACTGAGTCTACCA  
AAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGA CAAGTCTTTTCATGTGGTTTTTCT  
ACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC  
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA  
AACAGTGTACTATTCTGTGGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT  
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC  
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG  
GAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGA  
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC  
CTTGTTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG  
GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA  
CATTCGTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA  
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCCTTGTGGCTTCATGCTGATCCTTGT  
GGTCGTGCCACTGTTGCTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG  
TGGTCCCTCCAGACACCTTGAAAATAACCAATTCACCCAGAAAGTTAATCAGCTGCAGAAGG  
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT  
CTCATAGGTTTTCGGAAGGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC  
ATGAGGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA  
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC  
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC  
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC  
TACACACCTGCTAAACACACACACACAGAGTCTCTCTCTATATATACACACGTACACATAAA  
TACACCCAGCACTTGCAAGGCTAGAGGGAACTGGTGACACTCTACAGTCTGACTGATTCAG  
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT  
GGCTTGGAGAGCCCCTTTCCCAGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG  
TGTTGAGTTCACCTCAAGCCCAATGCCGGTGACAGGGGAATGGCTTAGCGAGCTCTACAGT  
AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC  
CATGAACTACTGTAAAGTGTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT  
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC  
TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA  
AAAAA

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**FIGURE 117**

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGE  
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDITATVPYNLRVRATLGSQTSW  
SILKHPFNRNSTILTRPGMEITKDGFLVIELEDLGPQFEFLVAYWRREPGAEHVKMVRSG  
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMILIV  
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

**Important features:****Signal peptide:**

amino acids 1-29

**Transmembrane domain:**

amino acids 230-255

**N-glycosylation sites.**

amino acids 40-43 and 134-137

**Tissue factor proteins homology.**

amino acids 92-119

**Integrins alpha chain protein homology.**

amino acids 232-262

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**FIGURE 118**

TCCTGCTGATGCACATCTGGGTTTGGCAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT  
CCTGGCCGGCTCTAGAACAATTCAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA  
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGG  
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT  
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC  
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA  
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTCTGAATACCAGGGGGAGTACGAGAGCCT  
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG  
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTCAGGGCCACATTGGGC  
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTAC  
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG  
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG  
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCCAC  
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTTGAT

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**FIGURE 119**

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGGCGTG  
GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG  
TCAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG  
AATGTGGCCAGCGAGTGCGGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG  
AGACCTGGGCCCCCACCACCTTTAACGTGCTCGCCTTCCCCCTGCAACCAGTTTGGCCAACAGG  
AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCC GCCGACCTACAGTGTCTCATTCCCC  
ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA  
GACTTCTGGGAAGGAGCCACCTGGAACCTTCTGGAAGTACCTAGTAGCCCCAGATGGAAAGG  
TGGTAGGGGCTTGGGACCCAACCTGTGTCACTGGAGGAGGTCAGACCCAGATCACAGCGCTC  
GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTATTAACCACCGCGTCTCCTCCTCCACCA  
CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACCTCAAATGGTGCTTCAAAGGGAG  
AGACCCACTGACTCTCCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA  
AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG  
AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAAA  
TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC  
CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC  
CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATAACTTGTTATCAAT  
AAAACTTGCAATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT  
GTTATTTCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA  
AACAATACCTCACGATATAAAATAAAAATGAAAGTATCCTCCTCAAAAA



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**FIGURE 120**

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLVKYRGSVSLVNVASECGFTDQ  
HYRALQQQLQORDLGPHHFNVLAFCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG  
AHPAFKYLAQTSGKEPTWNFWKYLVPDVGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

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**FIGURE 121**

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCCATGGGCTGTCTACGTCGGGATGC  
TGC GCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGCCCCGGGCCGCCCTCTCT  
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG  
CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTTCAGGGGTGCACCAAAAAGCATCTTA  
ACAGCAAGACTGTGGGCCAGTGCCTGGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGCC  
TTGGTCGTCTCCATGAAGACGTGAGGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA  
AGCTGCTTCTGGCCTCCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGGCATGTGGGGAC  
CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCAGGCGGGCATCATTCTGGTG  
TCTGTGAACCCAGCCTACCAGGCTATGGAAGTGGAGTATGTCTCAAGAAGGTGGGCTGCAA  
GGCCCTTGTGTTCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCTGAAGCAGATCT  
GTCCAGAAGTGGAGAATGCCCAGCCAGGGGCCTTGAAGAGTCAGAGGCTCCCAGATCTGACC  
ACAGTCATCTCGGTGGATGCCCCCTTTGCCGGGGACCCCTGCTCCTGGATGAAGTGGTGGCGGC  
TGGCAGCACACGGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCTGTCTGCCATG  
ACCCCATCAACATCCAGTTCACCTCGGGGACAACAGGCAGCCCCAAGGGGGCCACCCTCTCC  
CACTACAACATTGTCAACAACCTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC  
ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCTGTACCATTGCCTGGGTTCCTGTGGCAG  
GCACAATGATGTGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC  
AAGAAGGCACTGGAGGGCCATCAGCAGAGAGAGAGGCACCTTCTGTATGGTACCCCCACGAT  
GTTCTGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG  
GTGTCAATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT  
ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCCTGACATTCGCGCACTT  
CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGG  
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGGAGCTGTGC  
ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT  
GGATCAGGACAAGTGGTATTGGACAGGAGATGTGCCACAATGAATGAGCAGGGCTTCTGCA  
AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG  
CTCGAGGACTTCTTTCACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA  
CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTCCGGCTGAAGGACGGGGAGGAGACCACGG  
TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCCGAAGTACATC  
GTGTTTGTACAAACTACCCCTCACCATTTTCAGGAAAGATCCAGAAATTCAAACCTTCGAGA  
GCAGATGGAACGACATCTAAATCTGTGAATAAAGCAGCAGGCCTGTCTGGCCGGTTGGCTT  
GACTCTCTCCTGTCAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCCAGCACCCAGTTC  
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAACTAAGAGCTCCTGGATGGGTC  
CGGGAACCTCGCCTGGGCACAAGGTGCCAAAAGGCAGGCAGCCTGCCCAGGCCCTCCCTCCTG  
TCCATCCCCCACATTCCCCTGTCTGTCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT  
GAAAAAAAAAAAAAAAAA

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**FIGURE 122**

MAVYVGMLRLGRLCAGSSGVLGARAALSRWQEARLQGVRFLSSREVD RMVSTPIGGLSYVQ  
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG  
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY  
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN  
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY  
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY  
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG  
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT  
MNEQGFCIKIVGRSKDMIIRGGENIYPAELEDFHHTHPKVQEVQVVGKDDRMGEEICACIRL  
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domains:**

amino acids 140-161, 213-229, 312-334

**Putative AMP-binding Domain Signature:**

amino acids 260-271

**N-myristoylation Sites:**amino acids 19-24, 22-27, 120-125, 203-208, 268-273, 272-277,  
314-319, 318-323, 379-384, 380-385, 409-413**N-glycosylation Site:**

amino acids 282-285

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**FIGURE 123**

CAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA  
TGATCCTGCCCCAACCCCTGTACCATTGCCTGGGTTCCTGGCAGGCACAATGATGTGTCTG  
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGCAAGAAGGCACTGGAGGC  
CATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGATGTTCTGTGGACATTCTGA  
ACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAGGTGTCATTGCTGGGTCC  
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT  
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTTCCCTGAGGACACTGTGG  
AGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGGCGCGGATCATGAACATG  
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGAGCTGTGCATCCGAGGGTACTGCGT  
CATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT  
ATTGGACAGGAGATGTCGCCAC

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**FIGURE 124**

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGC  
AGGCTGGCTGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG  
TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC  
GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC  
AGTGCGGGGTTGCGGTTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC  
TTCTGGCGTTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC  
ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCAACGGCGTGAGTG  
CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCGTGAGCT  
GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTACCTTGACGGCA  
GCTAATGTGACTGTGTCTTGCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA  
TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAAC  
CTGACCTCCGCAACAAGACCTACTTCTCCCCTCGAATCCCACCCCTTGTCCGGCTGCCCCCT  
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCAACCACTTCTACCTCGGCCCCAGTGAG  
ACCCACATCCACCACCAAACCCATGCCAGCGCCAACCACTCAGACTCCGAGACAGGGAGTAG  
AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC  
CGCAGCAATTACGGGCAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCATAATAAAGGCTG  
TGTGGCTCCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCTACTGTG  
GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT  
CATCACTTCCTGTTCCCACCACTGGACTGGGCTGGCCCAGCCCCCTGTTTTTCCAACATTCCC  
CAGTATCCCCAGCTTCTGCTGCGCTGGTTTGCGGCTTTGGGAAATAAAATACCGTTGTATAT  
ATTCTGCCAGGGGTGTTCTAGCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC  
TCCGCTTGTCTCTTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTCACGGGGAAGGTG  
AGAGAGAGGATGCTAAGCTTCCTACTCACTTTCTCCTAGCCAGCCTGGACTTTGGAGCGTGG  
GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG  
GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCCGGTAC  
CCAATTCGCCCTATAGTGAGTCGTA

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**FIGURE 125**

MDPARKAGAQAMIWTAGWLLLLLLRGGAQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCT  
EAVGAVETIHGQFSLAVRGCGLPGKNDRGLDLHGLLAFIQLQOCAQDRCAKLNLTSRAL  
DPAGNESAYPPNGVECYSCVGLSREACQGTSPVVSVCYNASDHVYKGCFDGNVTLTAANVTV  
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPLVRLPPPEPTT  
VASTTSVTTSTTSAPVRPTSTTKPMPAPTSQTPRQGVHEASRDEEPRLTGGAAGHQDRSNG  
QYPAKGGPQQPHNKGCVAPTAGLAALLAVAAGVLL

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**FIGURE 126**

CGGGACTCGGCGGGTCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCC**ATGGAGT**  
TGGTGCTGGTCTTCCTCTGCAGCCTGCTGGCCCCCATGGTCCTGGCCAGTGCAGCTGAAAAG  
GAGAAGGAAATGGACCCTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGTT  
CGCTGTGGTCTCTTCTCGGTGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT  
TCAATCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCC  
AATGCAACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAA  
CCTGAGGCGGCTGCTTGAACCTTTGGATGCAAATGTCGATGCT**TAA**GAAAACGGGCCACTTC  
AGCAACAGCCCTTTCCCCAGGAGAAGCCAAGAACTTGTGTGTCCCCACCCTATCCCCTCTA  
ACACCATTCCTCCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGGTCTT  
GCCACCTCCCGTGATGTGTGTGTGTGTGTGTGTGTGTGACTGTGTGTGTTTGCTAACTGTG  
GTCTTTGTGGCTACTTGTGTGTGGATGGTATTGTGTTTGTAGTGAAGTGTGGACTCGCTTT  
CCCAGGCAGGGGCTGAGCCACATGGCCATCTGCTCCTCCCTGCCCCCGTGGCCCTCCATCAC  
CTTCTGCTCCTAGGAGGCTGCTTGTGCCCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGC  
GTAGGGTAAGAGCACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCAC  
TTTGTATCATTTCTTCATGGACTCCTTTCACTCCTTTAACAACAAACCTTGCTTCCTTATCCC  
ACCTGATCCCAGTCTGAAGGTCTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGAGCC  
CAGCGTTGACGTGAGGCAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGCTTCCACG  
AGGAGTCCCCATCTGCCCCGCCCCCTTACAGAGCGCCCCGGGGATTCCAGGCCCAGGGCTTCT  
ACTCTGCCCTGGGGAATGTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGG  
GACCCTACCCCTTCCAACCTTCCCTGCTTCTGAGACTTCAATCTACAGCCCAGCTCATCCAG  
ATGCAGACTACAGTCCCTGCAATTGGGTCTCTGGCAGGCAATAGTTGAAGGACTCCTGTTCC  
GTTGGGGCCAGCACACCGGGATGGATGGAGGGAGAGCAGAGGCCTTTGCTTCTCTGCCTACG  
TCCCCTTAGATGGGCAGCAGAGGCAACTCCCGCATCCTTTGCTCTGCCTGTGCGGTGGTCAGA  
GCGGTGAGCGAGGTGGGTTGGAGACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAG  
GTTGAAGGTCATAACGAGAGTGGGAACCAACCCAGATCCCGCCCCCTCCTGTCTCTGTGTT  
CCCGCGGAAACCAACCAACCGTGCGCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTAT  
CCTCAACAACAACAGAAAAAAGGAATAAAATATCCTTTGTTTCCT

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**FIGURE 127**

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRCK  
CSFNQKPRAPGDDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRLLLEPLDANVDA



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**FIGURE 128**

AAACTTGACGCCATGAAAGATCCCGGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT  
CCTCTGCCCAGGGAGCCACCCTGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG  
CGTCACGACCCGAGGCCTTTAACACCCCGTTCCTGAACATCGACAAATTGCGATCTGCGTTT  
AAGGCTGATGAGTTCCTGAACTGGCACGCCCTCTTTGAGTCTATCAAAGGAACTTCCTTT  
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCCAGT  
GACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT  
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTTCCATCCAAA

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**FIGURE 129**

MKIPVLPVAVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE  
FLNWHALFESIKRKLPFLNWDAFPKLKGLRSATPDAQ

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**FIGURE 130**

CAGTTCTGAAATCAATGGAGTTAATTTAGGGAATACAAACCAGCCATGGGGGTGGAGATTGC  
CTTTGCCTCAGTGATTCTCACCTGCCTCTCCCTTCTGGCAGCAGGAGTCTCCCAGGTTGTTC  
TTCTCCAGCCAGTTCCAACCTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC  
TTTGCCGGCCACTCATGAGAGTGTTTTTGTGTAAAGTATTTTTTTAGAATACTGTTGACTTCT  
TCATGATTTAATAACCATCCTTTGCGAAGTTTTATGAGGCTTTAGGGGAATGTCAACCCCTCA  
AATTTTTGTTATACTAGATGGCTTCCATTTACCCACCACTATTTTAAGGTCCCTTTATTTTT  
AGGTTCAAGGTTCAATTTGACTTGAGAAAGTGCCCTTCTGCAGCTTCATTGATTTTGTATC  
TTCATATTAATTGTAACGATTAAAAAGAATAAGAGCACGCAGACCTCTAGGAGAATATTT  
TATCCCTGGGTGCCCCTGACACATTTATGTAGTGATCCCACAAATGTGATTGTTAATTTAAA  
TGTTATTCTAATATTAGTACATTCAGTTGTGATGTAATATGAATAACCAGAATCTATTTCTT  
AAAAGTTTTGAGTATATTTTTCAACTAGATATTTGTATAGAAAGACTGAATAGTGATG

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**FIGURE 131**

MGVEIAFASVILTCLSLAAGVSQVLLQPVPQTQETGPKAMGDLSCGFAGHS

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**FIGURE 132**

GGGGAATCTGCAGTAGGTCTGCCGGCGATGGAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG  
GCTGCTGTTGTTCCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAAATGGA  
AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC  
TGCAGCTGCTACCATGGTGT CATAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG  
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA  
GACTGTACCGGGAAAATGACTGCATGTTCCCTCAAGGTGTAGTGGTGTGAGCACTTTATT  
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA  
GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC  
ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGACCTGCTGTTTGGCCAATTTAT  
CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTGAGCAGCACAGTG  
GCCATGGAAAAAGAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG  
ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACCTTGTTGATGCAGAATACACCAAAAAC  
CAGGCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT  
GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA  
AACACCTCTTCCTGTGTGGCTCACTTGTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC  
TATCCACAGCTGAAGCCATGGGTTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA  
AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA  
GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG  
AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT  
TCCCAAAATGTTGAAAACCTGAACTATAGTAGTCATCATAGGACCATAGTCCTCTTTGTGGCA  
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA  
TCTGCTATCAAGCCAAATACCTGGTTTTCTTATCATGCTGCACCCAGAGCAACTCTTGAGA  
AAGATTTAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTTGGATGAATAAGGA  
CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTCATTTTCTTAAGACCAATC  
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA  
TGTGATGATGCCCTTTGTCCCATTTTGGAGCAGAAAATTCGTCATTTGGAAGTAGTACAA  
CTCATTGCTGGAATTGTGAAATTATTCAAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG  
AAACCCATATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG  
TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAAAACCATAAACTCTGTTACTCAG  
GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT  
TCAGGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

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**FIGURE 133**

MEWWASSPLRLWLLLFLLP  
SAQGRQKESGSKWKVFIDQ  
INRSLENYEPCSSQNCSCY  
HGVIE  
EDLTPFRGGISRKMMAEV  
VRRKLGTHYQITKNRLYRE  
NDCMFPSRCSGVEHFILEV  
IGRLPD  
MEMVINVRDYPQVPKWME  
PAIPVFSFSKTSEYHDIMY  
PAWTFWEGGPAVWPYPTGL  
GRWDL  
FREDLVRSAQWPWKKKNST  
AYFRGSRTSPERDPLILLS  
RKNPKLVD AEYTKNQAWKS  
MKDT  
LGKPAAKDVHLVDHCKYK  
YLFNFRGVAASFRFKHLFL  
CGSLVFHVGDEWLEFFYPQ  
LKPVWH  
YIPVKTDLSNVQELLQFVK  
ANDDVAQEIAERGSQFIRN  
HLQMDDITCYWENLLSEYS  
KFLSY  
NVTRRKG YDQIIPKMLK  
TEL

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**FIGURE 134**

CACCCCTCCATTCTCTCGCCCATGCCCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT  
TCATCCTGGCCTTTGGCACCGGAGTGGAGTTTCGTGCGCTTTACCTCCCTTCGGCCACTTCTT  
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCCGCCAGGGATGGCTGGCTGCCCTGCAGGA  
CCGCAGCATCCTTGCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC  
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCCTTCAG  
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGCACTGGTGGTACTGGGAGCC  
CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC  
TCCTCTGCTTTGTGCTCCATGTCATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT  
GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC  
TCTGGCCCTGAAGTCTCCCCGGGCTCTCAGACTCTTCTCCACCTGCGCCACCCAGTGTGTG  
TGGAGCTGCTGACAGTGTGTGGGTGGTGCCTACCCTGGGCACGGACCGTCTCCTCCTTGCT  
TTCCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT  
CCGGGCCCAGCTACAAAGAAAACCTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT  
GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCTCCTCTCCCACTGAATTCTAAATCCTTAAC  
ATCCAGGCCCTGGCTGCTTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCTT  
CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA  
CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC  
TTCCTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC  
CTGACCACTCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCTTCTGCACCGCT  
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA  
GGCCCCAACCTTGCTCACCCTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT  
GGGCTCAGACCCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC  
CCTGCTCTCCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTTTTCTAAAAAAA

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**FIGURE 135**

MAPALLLIPAAALASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP  
LAWDLGLLLLFVGQHSLMAAERVKAWTSRYFGVLQRSLYVACTALALQLVMRYWEPIPKGPV  
LWEARAEPWATWVPLLCFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP  
RALRLFSLRHPVCVELLTVLWVPTLGTDRLLLAFLTLYLGLAHGLDQQDLRYLRAQLQR  
KLHLLSRPQDGEAE

**Signal sequence:**

amino acids 1-13

**Transmembrane domains:**

amino acids 58-76, 99-113, 141-159, 203-222

**N-myristoylation sites:**

amino acids 37-43, 42-48, 229-235



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**FIGURE 136**

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA  
AGAAATTGCCAAACCATGTCTTTTTTCTGTTTTTCAGAGTAGTTCACAACAGATCTGAGTGT  
TTTAATTAAGCATGGAATACAGAAAACAACAAAAAACTTAAGCTTTAATTTTCATCTGGAATT  
CCACAGTTTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTTCCCGCTGGCTGCTCTA  
TCACGTGGTGCTCTCCGACTACTCACCCCGAGTGTAAGAACCTTCGGCTCGCGTGCTTCTG  
AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCTTCCGAGTAGGATGTCACTGAGATCC  
CTCAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT  
TCCCCACTACAATGTGATAGAACGCGTGAAGTGGATGTACTTCTATGAGTATGAGCCGATTT  
ACAGACAAGACTTTCACCTTCACACTTCGAGAGCATTCAAAGTCTCTCATCAAAATCCATTT  
CTGGTCATTCTGGTGACCTCCCACCCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC  
TTGGGGTGAAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG  
AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTTATGGT  
GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTTATGGC  
ATTCAGGTGGGTAACTGAGTTTTGCCCAATGCCAAGTACGTAATGAAGACAGACACTGATG  
TTTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT  
TTCACAGTTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT  
TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTTATATAA  
TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGTACGTAATAACCCATCAAGTTT  
GAAGATGTTTATGTCGGGATCTGTTTGAATTTATTAAAAGTGAACATTCATATTCCAGAAGA  
CACAAATCTTTTCTTTCTATATAGAATCCATTTGGATGTCTGTCAACTGAGACGTGTGATTG  
CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTTTTGGCAGGTCATGCTAAGGAACACC  
ACATGCCATTATTAACTTCACATTCTACAAAAAGCCTAGAAGGACAGGATACCTTGTGGAAA  
GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG  
AACTGAAACTCATGAAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC  
AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGCTAAA  
GAAATTAATAGGACCAAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGG  
TGTTACTGAGTTATAAGCTCACTAGGCTGTAAAAACAAAACAATGTAGAGTTTTATTTATTG  
AACAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA  
TGTAAGTTCTGTGTCAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT  
TGGTCATTTATAAAGTACTTCAAGATGTTGCAGTATTTTACAGTTATTATTATTTAAAATTA  
CTTCAACTTTGTGTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAGGATAGTGAAT  
CATTCTTTACATGCAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC  
TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTAAAT  
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAA

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**FIGURE 137**

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPYRQD  
FHFTLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFLLGQEA EK  
EDKMLALSLEDEHLLYGDIIRQDFLDTYNNLTLKTIMAFRWVTEFCPNAKYVMKTDTDVFIN  
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD  
LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG  
FSSKEIITFWQVMLRNTTCHY

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**FIGURE 138**

CCTCTGTCCACTGCTTTTCGTGAAGACAAGATGAAAGTTCACAATTGTCTTTGCTGGACTTCTT  
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA  
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA  
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC  
AGACTCTTTCAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT  
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC  
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA  
AAAAACATTGCAAACATGTGTCTGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC  
AAGCCTGTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT  
CCTTCTGTGGAGACACGGTGGAGAACTAAACAATTTTTTAAAGCCACTATGGATTTAGTCAT  
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTACCATGTCATTCTGAAATT  
TTTCTCTACTAGTTATGTTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAAA

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**FIGURE 139**

MKFTIVFAGLLGVFLAPALANYNINVNDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS  
IWDYGNGFAATRLFQKKTCTIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPPKGLMYSVN  
PNKVDDLKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

**Signal Peptide:**

amino acids 1-20

**N-myristoylation Sites:**

amino acids 67-72, 118-123, 163-168

**Flavodoxin protein homology:**

amino acids 156-174

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**FIGURE 140**

CATTTCTGAACTAATCGTGTCAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA  
TTAACTTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG  
CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTCTTATTGCTTACTGATTTTTT  
TGAGTTAAGAGTTGTTATATGCTAGAAATATGAGGATGTGAATATAAATAAGAGAAGAAAAA  
GAATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTTTACATG  
CAAGCTTATAGTTGAAATATTTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGT  
TTGTTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT  
CAGATTCCGTTGCCAACTCGTCCCCATTGGTTTCTTCTTTTTGGTACTACAGAAGAGGAAAT  
CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAGCCAACTATGAATTAC  
TGGAAAAAGAAGTAGAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTTAAAGCAAAGGGA  
TTGAATCCGGATGGAAGTCCAGCCCTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC  
ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG  
TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCAAAAAGCCCTTACAATGGTGTAAGAAAA  
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAAGTCGATCGAGGTCAAGAACACGATCACG  
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA  
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT  
GGTTCTCCTCACCTTAAGGCCAAGCATACCAGAGATGATTTAAAAAGTTCAAACAGACATGG  
TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG  
CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT  
GAGAGGTCCCATAAAAGCAAGCACCATGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG  
CTGACTTTCTCTTCCTTTGAGCCTGCATCAGTTCTTGGTTTTGCCTATCTACAGTGTGATGT  
ATGGACTCAATCAAAAACATTAAACGCAAACCTGATTAGGATTTGATTTCTTGAAACCCTCTA  
GGTCTCTAGAACACTGAGGACAGTTTCTTTTGAAAAGAACTATGTTAATTTTTTTGCACATT  
AAAATGCCCTAGCAGTATCTAATTA AAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT  
TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT  
ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT  
ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTTACAAGGAAATAAAATACAAAT  
CTTGTTTTTTCTAAAAA AAAAAAAAAAAAAAAGT

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**FIGURE 141**

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLFSGTTEEEIQEICIETLRLY  
TRKKPNYELLEKEVEKRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEEK  
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN  
NRRSRSGTYSSRSRSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRKKSRSRSQ  
SKSRDHSDAAKKHRHERGHHRDRRERSRSFERSHKSKHHGGSRSRSGHGRHRR

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**FIGURE 142**

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTTATCA  
TTTTTTGAANNNTATTCGGGTCANAATTGNCTTTGAAAAGCATTGCTTTTTACAGAAATATAT  
TANCTTTTTAGAGTAATTTCTAGTTTGGATTGTAATATGAAATTATTTAAAAGGGCTTCGCT  
CATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTNTTATTGCTTACTGATTTTTTTTG  
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAGA  
ATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTTTACATGCA  
AGCTTATAGTTGAAATATTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGTTT  
GTTTCGATTTCAACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAGNTAGAGCACTTCA  
GATTCCGTTGCCAACTNGTCCCCATTGGTTTCTTCTTTTGGTACTACAGAAGAGGAAATCC  
AGGAAATNTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAACTATGAATTACTG  
GAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCNAATTAAAAGCAAAGGGATT  
GAATCCGGATGGAACCTCAGCCCTTTCAACCCTGGGTGGATTTTCTCC

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**FIGURE 143**

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGCACCGCGTTCTCGCACGCGTCCATGGC  
GGTCCTCGGAGTACAGCTGGTGGTGACCCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC  
CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTTTGTTCGGATAACAAGCACCCG  
TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG  
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG  
AGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCTGCGCTTCTTCCTGGAGTACCAGTGG  
TTTGTGGAÇTTTGCTGTGTACTCGGGCGGCGTGTACCTCTTCACAGAGGCCTACTACTACAT  
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCTGCTCACGGTGACCTTCT  
CCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGTGAGCGC  
TCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG  
GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC  
CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG  
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC  
CCAGACCCACCGGGACGCACTGACCATGTCGGAGGACAGACCCATGCTGCAGTTCCTCCTGC  
ACACCAGCTTCCTGTCTCCCCGTGTTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC  
TTCCTGCACCAGCCGCCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA  
CTCTGGGCGCCTCTGGTTGCTGGTGGTGTGTGCCTGCTGCGGCTGGCGGTGACCCGGCCCC  
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC  
CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT  
GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCCCTCAACTGCACACTTCTGCTCAAGACGC  
TGGGAGGCTATTCTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCGACCCATCCTCAGCC  
AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG  
GGCCCTGGGTGGCCTGCTTACTCCCCTCTTCCTCCGTGGCGTCCTGGCCTACCTCATCTGGT  
GGACGGCTGCCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA  
GGCTCCTAGCTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCTGGGGCAGCGGGACA  
CTAGCCTGCCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC  
GGCGTTCCCTTCACCACAGTGCTGACCCGCGGCCCCCCCTTGGACGCCGAGTTTCTGCCTCA  
GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG  
TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC  
GATTTTAA



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**FIGURE 144**

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE  
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY  
YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV  
VREETLELGLPGLASMTQNLEPLLKKQGWDWALPVAKLAIRVGLAVVGSVLGAFLTFFGLR  
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA  
FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT  
VVSLLQYLTPILTLNCTLLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAAARI  
AGALGGLLTPLFLRGVLAYLIWWTAAACQLLASLFGLYFHQHLA

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**FIGURE 145**

CGTTNGCACGCGTCAATGGCGGTCCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCAC  
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTT  
TGTTCCGATACAAGCACCCGTNTTGAGGAGGAGCTTCGGGGCCCTGGCGGGGAAGCCGAGGCC  
CAGAGGCAGGAAAGAGCGGTGGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCC  
GAGATGCCCCGTTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCCTGCGC  
TTCTTCCTGGAGTACCAGTGGTTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGTACCTCTT  
CACAGAGGCCTACTACTACATGCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT  
GCCTGCTCACAGTGACCTTCTCCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGC  
GCCGAGGAGGGGGGTGAGCGCTCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGC  
CATGCTGGTGCAAGCG

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**FIGURE 146**

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCCGTGATTTATTAACGTGGCTT  
AATCTGAAGGTTCTCAGTCAAATCTTTGTGATCTACTGATTGTGGGGGCATGGCAAGGTTTGCTTAAAGGAGC  
TTGGCTGGTTTGGGCCCTTGTAGCTGACAGAAGGTGGCCAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGG  
CGCTTCTGTTGCTGGTCTTGCTTGGCTCAGTCTGCTAACTACATTGACAATGTGGGCAACCTGCACTTCCTG  
TATTCAGAACTCTGTAAAGGTGCCTCCCACTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTG  
TCCAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCTCCCCAGAGGTTTCTGCAGCTGCCACCATCTCCTTAA  
TGACAGACGAGCCTGGCCTAGACAACCTGCCTACGTGTCTCGGCAGAGGACGGGCAGCCAGCAATCAGCCCA  
GTGGACTCTGGCCGGAGCAACCGAACTAGGGCACGGCCCTTGTAGAGATCCACTATTAGAAGCAGATCATTTAA  
AAAAATAAATCGAGCTTTGAGTGTTCTTGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGG  
GCAGGGAAAATTCTGAAAACACCACTGCCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCAGATGGTGAA  
ATTACCAGCATCAAGATCAATCGAGTAGATCCCACTGAAAGCCTCTCTATTAGGCTGGTGGGAGGTAGCGAAAC  
CCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAGAGACGGCCGGCTACTGCCAG  
GAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATGTCCCTCACAACCTACGCTGTGCGTCTCCTGCGG  
CAGCCCTGCCAGGTGCTGTGGCTGACTGTGATGCGTGAACAGAAGTCCCGCAGCAGGAACAATGGACAGGCCCC  
GGATGCCATACAGACCCCGAGATGACAGCTTTCATGTGATTTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGAA  
TAAACTGGTGCGCAAGGTGGATGAGCCTGGGGTTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCATATCGA  
CATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCGATATGGCAGCCCAGAAAG  
TGCGGCTCATCTGATTACAGGCCAGTGAAAGACGTGTTACCTCGTGTCCCGCCAGGTTCCGCGAGCGGAGCC  
CTGACATCTTTCAGGAAGCCGGCTGGAACAGCAATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGGAGCAACACT  
CCCAAGCCCCCTCCATCCTACAATTACTTGTCTGATGAGAAGGTGGTAAATATCCAAAAGACCCCGGTGAATCTCT  
CGGCATGACCGTCGACGGGGGAGCATCACATAGAGAATGGGATTTGCCTATCTATGTCTCAGTGTTGAGCCCG  
GAGGAGTCATAAGCAGAGATGGAAGAATAAAAACAGGTGACATTTTGTGTAATGTGGATGGGGTCGAACTGACA  
GAGGTCAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCATCCTCGATAGTACTCAAAGCTTTGGAAGT  
CAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGCCCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCA  
GTGACTGGTCCCCATCCTGGGTCTATGTGGCTGGAATTACCACGGTGCTTGTATAACTGTAAAGATATTGTATTA  
CGAAGAAACACAGCTGGAAGTCTGGGCTTCTGCATTGTAGGAGGTTATGAAGAATAAATGGAACAAACCTTT  
TTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGGTGATATTCTTCTTG  
CTGTCAATGGTAGAAGTACATCAGGAATGATACATGCTTGCTTGGCAAGACTGCTGAAAGAACTTAAAGGAAGA  
ATTACTCTAACTATTGTTTCTTGGCCTGGCACTTTTTTATAGAATCAATGATGGGTCAGAGGAAAACAGAAAAA  
TCACAAATAGGCTAAGAAGTTGAAACACTATATTTATCTTGTCAGTTTTTATATTTAAAGAAAGAATACATTGT  
AAAAATGTCAGGAAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAATTA  
AACTACTAGTTTTTTTTTTCAGTGTGGAGGATTTCTATTACTCTACAACATTGTTTATATTTTTCTATTCAAT  
AAAAAGCCCTAAAACAATAAATGATTGATTTGTATACCCCACTGAATTCAGCTGATTTAAATTTAAATTT  
GGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCATTTTTAATTTACAGCTAAAATATTTTTTAAATGCA  
TTGCTGAGAAACGTTGCTTTTCATCAAACAAGAATAAATATTTTTTCAGAAGTTAA

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**FIGURE 147**

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPCDGCASLTAT  
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS  
FKKINRALSVLRRTKSGSAVANHADQGRESENTTAPEVFPRLYHLIPDGEITSIKINRVDP  
SESLSIRLVGGSETPLVHIIIQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPBNYAVRLL  
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQGLGKLVKRVDEPGV  
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESAHLIQASERRVHLVVSQRQVRQRS  
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNIIQKDPGESLGMTVAGGASHRE  
WDLPIYVISVEPGGVISRDGRIKTDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV  
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV  
GGYEEYNGNKPFIFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI  
TLTIVSWPGTFL

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**FIGURE 148**

CCAAAGTGATCATTTGAAAAAGAGATATCCACATCTTCAAGCCCATATAAAGGATAGAAGCT  
GCACAGGGCAGCTTTACTTACTCCAGCACCTTCCTCTCCCAGGCAAATGGTGCTGACCATCT  
TTGGGATACAATCTCATGGATACGAGGTTTTTAACATCATCAGCCCAAGCAACAATGGTGGC  
AATG TTCAGGAGACAGTGACAATTGATAATGAAAAAAATACCGCCATCGTTAACATCCATGC  
AGGATCATGCTCTTCTACCACAATTTTTGACTATAAACATGGCTACATTGCATCCAGGGTGC  
TCTCCCGAAGAGCCTGCTTTATCCTGAAGATGGACCATCAGAACATCCCTCCTCTGAACAAT  
CTCCAATGGTACATCTATGAGAAACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG  
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCCTGCTTGGGTCAC  
CCATTGAGAACTCTGCAAACATATCCCTTTGTATAAGGGGGAAGTGGTTGAAAACACACAT  
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGGCTCCTGGGCATCTTGGGAATTTCAATCTG  
TGCAGACATTCATGTTTAGGATGATTAGCCCTCTTGTTTTATCTTTTCAAAGAAATACATCC  
TTGGTTTACACTCAAAAGTCAAATTAAATTCTTTCCCAATGCCCCAACTAATTTTGAGATTC  
AGTCAGAAAATATAAATGCTGTATTTATA

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**FIGURE 149**

MKILVAFLVVLTIQSHGYEVFNIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT  
IFDYKHGYIASRVLSRRACFILKMDHQNIPPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE  
SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

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**FIGURE 150**

GGCACGAGCCAGGAAGTAGGAGGTTCTCACTGCCCCGAGCAGAGGCCCTACACCCACCGAGGC  
**ATG**GGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG  
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTCCCCAAAG  
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCAGCCACCACCGCCCATCACCTATTCCCTC  
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGGCCTCCTT  
CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT  
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG  
CCAGTGTCTGAGCTGCGGGCCAACCTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA  
GATGATCTGCCAGGCGTCCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAGGATG  
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCCTGCCG  
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC  
CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA  
GCCCCATCCTTGCCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG  
GGGTTCAGGATAGGGAATGGGGAGGTCAGAGGACGCAAAGCAGCAGCCATG**TAGA**ATGAACC  
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTCTGTTTGGGA  
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 151**

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVPKGRWVLITCCAPQPPPPITYSL  
CGTKNIKVAKKVVKTHEPASFNLVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK  
PVSELNANFTLQDRGAGPRVEMICQASSGSPITNSLIGKDGQVHLQQRPCHRQPANFSFLP  
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG  
GFRIGNGEVRGRKAAAM

**Signal Peptide:**

amino acids 1-18

**N-glycosylation Sites:**

amino acids 86-89, 132-135, 181-184



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**FIGURE 152**

GGTCCTTAATGGCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG  
CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTCTTTGCTATGACATCACCGT  
CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA  
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGGAAGAAA  
CTAAATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT  
TACAGAGCAACTGCGTGACATTCAGCTGGAGAATTACACACCCAAGGAACCCCTCACCCCTGC  
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT  
TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC  
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT  
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC  
CTGGAGCCAAGTGCAGGAGCACCCTCGCCATGTCTTCAGGCACAACCCAACCTCAGGGCCAC  
AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA  
TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAGGCTCCTGTGAGCAGC  
GTCTTGATCAAACCTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT  
GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCCTT  
TTGCCAACAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGCTACC  
TGATGGAATTCCTGCACTTAAAGTTCTGGCTGACTAAACAAGATATATCATTTTCTTTCTTC  
TCTTTTGTGTTGGAAAATCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATT  
GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG  
AATTTTAAATTATTTAATAAGAAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTAT  
TGTTCTGTACTGATATTTAAATAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAA

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**FIGURE 153**

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTF  
HYDCGNKTVTPVSP LGKKLNVT TAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR  
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS  
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

**Important features:****Signal peptide:**

amino acids 1-25

**Transmembrane domain:**

amino acids 224-246

**N-glycosylation site.**

amino acids 68-72, 82-86

**N-myristoylation site.**

amino acids 200-206, 210-216

**Amidation site.**

amino acids 77-81

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**FIGURE 154**

GGGAAAGCCATTTGCGAAAACCCATCTATACAACTATATATTTTCATTTCTGCTGCTAGCTG  
CCTTGGGCCTCACAATTTTCATTCTGTTTTCTGACTTTCAAGTTATATACCGTGGAATGGAG  
TTGATCCCAACCATAACATCGTGGAGGGTTTTAATTTTGGTGGTAGCCCTCACCCAATTCTG  
GTGTGGCTTTCTTTGCAGAGGATTCCACCTTCAAAATCATGAACTCTGGCTGTTGATCAAAA  
GAGAATTTGGATTCTACTCTAAAAGTCAATATAGGACTTGGCAAAAGAAGCTAGCAGAAGAC  
TCAACCTGGCCTCCCATAAACAGGACAGATTATTCAGGTGATGGCAAAAATGGATTCTACAT  
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAATCAAATTGGGAGGCCAAC  
CCACAGAACAGCATTTCTGGGCCAGGCTGTAATCAGAATTGTCGTCGTACATGCTCAACAGC  
ATTGCTTTTTTCCCCAAAATTAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTTT  
CCTCTCTCCATTCAAGCATTCAAAGTATATTTTCAATGAATTAAACCTTGCAGCAAGGGACC  
TTAGATAGGCTTATTCTGACTGTATGCTTTACCAATGAGAGAAAAAAATGCATTTCTGTAT  
CATCCTTTTCAATAAACTGTATTTCATTTTGAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 155**

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHFWLLIKREFGFYSKSQYRTWQKKLA  
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL

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**FIGURE 156**

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAG  
CTCTTGTGGCAGGTAAGTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTTCGTCTA  
CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC  
AGAACTGCCCCCTCCGTTTGCTCGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCACGCGCCGG  
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA  
CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCTGCAGT  
TGGGCAGGAAGTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAAC  
ACCTTGGAGCTGTTTCGACAAGTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTC  
CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA  
ACCGGGTGCCCTCCCTCATGCGCCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT  
GAGGGAGCTTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA  
AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTGAGGGAACCACT  
TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTCATG  
AACTCACAGGTCAGCCTGATTGAGCGGAATGCTTTTGACGGGCTGGCTTCACTTGTGGAAGT  
CAACTTGGCCCAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC  
TGGTGGAGTTGCATCTACACCACAACCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC  
TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTCCCAT  
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT  
TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTTCGGATGGCAGAACTTAAGTGT  
CGGACTCCCCCTATGTCCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC  
CTCCCGCCACCCAAGGATCTCTGTCTCAACGACGGCACCTTGAACTTTTCCACGTGCTGC  
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG  
GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTCACCACAGT  
AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTTA  
CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTCAGACTACC  
CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT  
GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG  
CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC  
ACAGCCGCCCCGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGC  
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC  
ATGACCATATTAATACTACAACACCTACAAACCAGCACATGGGGCCCCACTGGACAGAAAACAGC  
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCA  
TACCAAGGACAAGGTACAGGAACTCAAATATTGACTCCCCCTCCCCCAAAAACTTATAAAAT  
GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTA  
TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAACAGATTATATTAATAATTTAAAGA  
CAAAAAGTCAAAACA

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**FIGURE 157**

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCT  
RRGLSEVPQGIPSNTRYLNLNMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS  
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY  
ISEGAFEGLFNLKYLNLGMCNIKDMPNLTPLVGLLEELEMSGNHFPFIRPGSFHGLSSLKKLW  
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLPHDLFTPLRYLVELHLHHNPWNCDCDILW  
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL  
KCRTPPMSSVKWLLPNGTVLSHASRHPRISVLNDGTLNFSHVLLSDTGVYTTCMVNTNVAGNSN  
ASAYLNVSTAELENSTSNYSFFTFTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ  
TTRVPKQVAVPATDTTDMQTSLEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS  
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE  
NSLGNSLHPTVTTISEPYIIQTHTKDKVQETQI

**FIGURE 158**

[illegible]

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**FIGURE 159**

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREVV  
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGTLDDFYVKGFYCAECRAGWYGGD  
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD  
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFSHSDGSKNFDGFAIYEEITACSSSPCFHDG  
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV  
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPQVQSRETPLH  
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK  
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE  
RTVVVAHCVTDLGKVTMIKTADLKVVLGKFYRDDDRDEKTIQSLQISAILHPNYDPILLD  
ADIAILKLLDKARISTRVQPICLAASRDLSTSFOESHITVAGWNVLADVRSPGFKNDTLRSG  
VVSVDSSLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR  
WHLMGLVSWSYDKTCSHRLSTAFTKVLFPKDWIERNMK



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**FIGURE 160**

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA  
AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAAACATGGGC  
TTCAACCTGACTTTCACCTTTCCTACAAATTCGGATTACTGTTGCTGTTGACTTTGTGCCT  
GACAGTGGTTGGGTGGGCCACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCTTAAAG  
CAAAGGAGTTCATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAGGGAAAACTCTGACT  
AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACTGTCCTTCTGTGTCTCCTTACCTCAG  
AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC  
CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATC  
CTCGTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTT  
CCTGCAGAGGCAGCAGCTGGATTATGGCATCTACGTCATCCACCAGGCTGAAGGTAAAAAGT  
TTAATCGAGCCAACTCTTGAATGTGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGAC  
TGCTTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGA  
GGAGCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTG  
GATATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCT  
AACAACCTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAG  
AATGAAAATTTCCCGGCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAG  
ACAAAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTACGAGTCTGG  
AGAACAGATGGGTTGAGTAGTTGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATA  
TATCAACATCACAGTGGATTTCTGGTTTGGTGCATTGACCCTGGATCTTTTGGTGATGTTTGG  
AAGAACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTA  
AGAACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCCTTTTGTATTTTCTTAGCAGAGCT  
CCTGGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTCTTAGTCATTTTGATCATG  
AGGGTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGAT  
AAAATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTTGAAGTAATATAT  
TATGGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCT  
CGTCCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTTCATTTATCCTGTACAATCATCT  
GTGAAGTGGTGGTGTGAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCA  
GGACACAGTGAACCTTGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGGCTGCAAAGGCAG  
CAGTAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCT  
TCCAGTGATGCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAATGA  
TTTTGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAATAATAATAATA  
TGTCTATCAAATACCTCTGTAGTAAAATGTGAAAAAGCAAAA

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**FIGURE 161**

MGFNLT FHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTLILGKGKT  
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV  
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKKFNRAKLLNVGYLEALKEEN  
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVLTALSREQFFKVNG  
FSNNYWGWGGEDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR  
VWRTDGLSSCSYKLVSV EHNPLYINITVDFWFGA

**Important features:****Signal peptide:**

amino acids 1-27

**N-glycosylation sites:**

amino acids 4-7, 220-223 and 335-338

**Xylose isomerase proteins:**

amino acids 191-201

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**FIGURE 162**

CGTGGGCCGGGGTTCGCGCAGCGGGCTGTGGGCGCGCCCGGAGGAGCGACCGCCGCAGTTCTC  
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGGCCCCGCAATG  
GCCCAGGCAGTGTGGTCGCGCCTCGGCCGCATCCTCTGGCTTGCCTGCCTCCTGCCCTGGGC  
CCCGGCAGGGGTGGCCGCAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA  
CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG  
CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA  
GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTGGCCACGTGCCCCGGGAATTCCCGG  
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG  
GTCCTCCCCATCACAGAGTTCCTCGTGGGGGACCTTGTTGTCAACCAGAACACTTCCCTACC  
CTGGCCCAGCTCCTATCTCACTAAGACCGTCTGAAAGTCTCCTTCCTCCTCCACGACCCGA  
GCAACTTCTCAAGACCGCCTTGTTTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG  
GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT  
CAAAGTGGTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA  
CCGGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTTGGGG  
CCCACCCTAATTACAGACCTTCCAAAAGATGACCGTGACCTTGAACCTCCTGGGGAGCCCTCC  
TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC  
CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCTGGGGACTAC  
TGCTTCAGCATCCGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT  
GTGGCCCTCCAGAATCCAGCCGGCTGTCTTTGCTTTCCCATGTGCTACACTTATCACTGTGA  
TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG  
AACCCGGAGCCACCTCTGGGGTCAGGTGCTGCTGCCAGATGTGCTGTGGGCCTTTCTTGCT  
GGAGACTCCATCTGAGTACCTGGAATTTGTTGCTGAGAACCACGGGCTGCTCCCGCCCCCTCT  
ATAAGTCTGTCAAAACTTACACCGTGTGAGCACTCCCCCTCCCCACCCCATCTCAGTGTTAA  
CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTTCAAT  
TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC  
CCTCCCTCTCTGTACCCCTGACCCAGCCATTACCCATCTGTACAGTCCAGCCACTGACA  
TAAGCCCCACTCGGTTACCACCCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT  
TTGATGCTTGGGGTGTTCCGTGTTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCATTCTCT  
CTCATATTGGCACATCTGCTGTCCATTGGGGGTTCTCAGTTTCTCCTCCCCCAGACAGCCCTAC  
CTGTGCCAGAGAGCTAGAAAGAAGGTCATAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC  
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACACA  
CACACACACAGAAATATAAACACATGCGTCACATGGGCATTTTCAAGATGATCAGCTCTGTA  
TCTGGTTAAGTCGGTTGCTGGGATGCACCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA  
AGCAGCCCTGACAGGTTCTGGGCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC  
GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCCTGGATGGGGGGCAGGACT  
AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG  
AACTTTCACTGAGGAAAAGGCCTTGACAGCGGTAGAAGAGGTTGAGTCAAGGCCGGGCGCGG  
TGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA  
GATCGAGACCACCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAATACAAAAAGTT  
AGCCGGGCGTGGTGGTGGGTGCCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG  
GTGCGAACCCGGGAGGCGGAGCTTGCAGTGAGCCAGATGGCGCCACTGCACTCCAGCCTGA  
GTGACAGAGCGAGACTCTGTCTCCA

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**FIGURE 163**

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA  
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGF  
VVLPITEFLVGDLVVTQNTSLPWSSYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDTQ  
MVTEDSVVYYNYSIIGTFTVKLVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL  
GPTLIQTFQKMTVTNLNFGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTFRDPGD  
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAPFCATLITVMLAFIMYMTLRNATQQKDMV  
ENPEPPSGVRCCCQMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

**Important features of the protein:****Signal peptide:**

amino acids 1-24

**Transmembrane domain:**

amino acids 339-362

**N-glycosylation sites.**

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367



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**FIGURE 165**

MALSSQIWAACLLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTH  
FPICIFCCGCCHRSKCGMCCKT

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**FIGURE 166**

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC  
CTGGATCTTCCACCATGTTTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC  
ATCTCCCTGACTGTCCTCTTACCCTCCTTCTCGTTTTTCATCATAGTGCCAGCCATTTTGG  
AGTCTCCTTTGGTATCCGCAAACCTCTACATGAAAAGTCTGTAAAAATCTTTGCGTGGGCTA  
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC  
GGAATCATTGCAAAGGATCCCCTTCACTAGAAGAAGAGATCAAAGAGATTCTGTCGAAGTGG  
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGCC  
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAAGTGG  
GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC  
GGTCCTGTGGGGGTAGGAGTGCTGATTCCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC  
TGGCTTTCACAGGGATTAGCCTTCTGGTGGTGGGCACAAGTGTGGTGGGATACTTGCCAAAT  
GGGAGGTTTAAAGGAATTCATGAGTAAACATGTTCACTTAATGTGTTACCGGATCTGCGTGGC  
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT  
GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC  
ATGGTGGGTCAAGTGCACGGGGGACTCATGGGTGTGATTCAGAGAGCCATGGTGAAGGCCTG  
CCCACACGTCTGGTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA  
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC  
AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC  
TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA  
TGGTGACGTACCTGCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG  
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGCGAATAGGGTGAAATCTGC  
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGGATGGGGGCCTGAAGAGGGAGAAGG  
TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACCAC  
AAGGACAGGAGCCGCTCCTTGAGCCTGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA  
CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCGCCACTGCTGTGTCCTTTCCAGACTCCAGGG  
CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT  
GCACCCGGCGCAGCCTACCCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA  
CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACCTCCCA  
CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT  
GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGCGGCCAECGG  
CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC  
CTTGAGCTCTGCAGACATGATAGGAAGGAACTGTCACTCTGCAGGGGCTTTTCAGCAAAATG  
AAGGGTTAGATTTTATGCTGCTGCTGATGGGGTTACTAAAGGGAGGGGAAGAGGCCAGGTG  
GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCTGTAATATGAGTGGGGG  
GAATGGTGGTGATTCCCTACCTCACAGGGCTGTTGTGGGGATTAAAGTGTGCGGGTGAGTGA  
AGGACACATCACGTTCAGTGTTTCAAGTACAGGCCCCACAAAACGGGGCACGGCAGGCCTGAG  
CTCAGAGCTGCTGCACTGGGCTTTGGATTTGTTCTTGTGAGTAAATAAACTGGCTGGTGAA  
TGA

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**FIGURE 167**

MFLLLPFDSLIVNLLGISLTVLFTLLLVFIIIVPAIFGVSTFGIRKLYMKSLKIFAWATLRME  
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRGSSKALDNTPEFELSDIFYFCRKGME  
TIMDDEVTKRFSAAEELSWNLLSRTNYNFQYISLRLTVLWGLGVLIRYCFLPLRIALAF  
TGISLLVVGTTVVGYPNGRFKEFMSKHVHLMCYRICVRAITAIITYHDRENRPNGGICVANH  
TSPIDVILASDGYAMVGQVHGGLMGVIQRAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ  
DKSKLPILIFPEGTCINNTSVMFMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMV  
TYL LRMMTSWAIVCSVWYLPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREK  
VKDTF KEEQQKLYSKMIVGNHKDRSRS



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**FIGURE 168**

GCCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCGCCCTCACCCGGACCCCTGGCCCTCA  
CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCCTCCAC  
ACCTGGCAGGCCCAGGCTGTTCCCACCATCCTGCCCCCTGGGCCTGGCTCCAGACACCTTTGA  
CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG  
AAATGGCCCACCATGCCCCTGCTGCGGGAATCCTGGGAGGCAGCCCAGGAGACCTGGGAGGAC  
AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT  
CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG  
GCTCCCGGGAGCTCTACATGAGGCACTTTCCTTCAAGGCCCTGCATTTCTACCTGATCCGG  
GCCCTGCAGCTGCTGCGAGGCAGTGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCGG  
AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT  
TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCACAGATTTGGGGAGAAGAGGCGGGGCTGT  
GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTCTGCCCCCTG  
GAAGACTCTGCTCTTGGCCCCCTGGAGAGTTCCAGCTCTCAGGGGTGGGGCCCTTGAAAGTCCA  
ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG  
CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCCAGG  
ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGGACTTCCT  
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGTTGCAATGTGGAGACA  
TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

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**FIGURE 169**

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH  
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSNTLYWELNQAVRTGGGSREL  
YMRHFPPKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS  
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLAPGEFQLSGVGP

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**FIGURE 170**

GTGGCTTCATTTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA  
CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG  
GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC  
TATTGTCTGGACCTTCAACACAACCCCTCTTGTACCATAACAGCCAGAAGGGGGCACTATCA  
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG  
CTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT  
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG  
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG  
GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC  
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT  
GCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT  
GAAGGTGCTGCTGATGACCCAGATTCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGCCCCCT  
CCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTCTGAAGAGAGAGAGACAAGAAG  
AGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAAACTCCTAACATATGCCCCCAT  
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA  
TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC  
TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATCTAGACAGCAGTG  
CACTCCCCTAAGTCTCTGCTCA

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**FIGURE 171**

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT  
IQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV  
YEHLSPKPKVTMGLQSNKNGTCVTNLTCMEHGEEVDVIYTWKALGQAANESHNGSILPISWRW  
GESDMTFICVARNPVS RNFS PILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW  
FLKRERQEEYIEEKKRVDICRETPNICPHSGENTEYDTIPHNTILKEDPANTVYSTVEIP  
KKMENPHSLLTMPDTPRLFAYENVI

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**FIGURE 172**

CTGGTTCCCCAACATGCCTCACCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC  
TCTGGACCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC  
CAAAGTAAAGCAAGTTGACTCTATTGCTCTGGACCTTCAACACAACCCCTCTTGTACCATAC  
AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA  
GATGGAGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT  
GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG  
AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG  
ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT  
GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG  
AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCC  
ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCCCTCCATGGTCCTCCT  
GTGTCTCCTGTTGGTGCCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC  
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAA  
ACTCCTAACATATGCCCCCATCTGAGAGAGAACACAGAGTACGACACAATCCCTCACACTAA  
TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA  
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG  
AATGTTATCTAGACAGCAGTGCACTCCCCTAAGTCTCTGCTCAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 173**

GAAAGACGTGGTCCTGACAGACAGACAATCCTATTCCCTACCAAAATGAAGATGCTGCTGCT  
GCTGTGTTTGGGACTGACCCTAGTCTGTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA  
ACTTTAATGTAGAAAAGATTAATGGGGAATGGCATACTATTATCCTGGCCTCTGACAAAAGA  
GAAAAGATAGAAGAACATGGCAACTTTAGACTTTTTCTGGAGCAAATCCATGTCTTGGAGAA  
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTTG  
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTTACT  
ATACCTAAGACAGACTATGATAACTTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGGA  
AACCTTCCAGCTGATGGGGCTCTATGGCCGAGAACCAGATTTGAGTTCAGACATCAAGGAAA  
GGTTTGCACAACTATGTGAGGAGCATGGAATCCTTAGAGAAAATATCATTGACCTATCCAAT  
GCCAATCGCTGCCTCCAGGCCCCGAGAATGAAGAATGGCCTGAGCCTCCAGTGTTGAGTGGAC  
ACTTCTCACCAGGACTCCACCATCATCCCTTCCTATCCATACAGCATCCCCAGTATAAATTC  
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCCAGTCTATCAACATGTTACC  
TAGGATACCTCATCAAGAATCAAAGACTTCTTTAAATTTCTCTTTGATACACCCTTGACAAT  
TTTTCATGAAATTATTCCTCTTCCTGTTCAATAAATGATTACCCTTGCACTTAA

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**FIGURE 174**

MKMLLLLCLGLTLVCVHAAEEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ  
IHVLENSLVCLKVHTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI  
NEKDGETFQLMGLYGREPDLSSDIKERFAQLCEEHGILRENIIDLSNANRCLQARE

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**FIGURE 175**

GGCTCGAGCGTTTCTGAGCCAGGGGTGACCATGACCTGCTGCGAAGGATGGACATCCTGCAA  
TGGATTGAGCCTGCTGGTTCTACTGCTGTTAGGAGTAGTTCTCAATGCGATACCTCTAATTG  
TCAGCTTAGTTGAGGAAGACCAATTTTCTCAAACCCCATCTCTTGCTTTGAGTGGTGGTTC  
CCAGGAATTATAGGAGCAGGTCTGATGGCCATTCCAGCAACAACAATGTCCTTGACAGCAAG  
AAAAAGAGCGTGCTGCAACAACAGAACTGGAATGTTTCTTTCATCATTTTTTCAGTGTGATCA  
CAGTCATTGGTGCTCTGTATTGCATGCTGATATCCATCCAGGCTCTCTTAAAAGGTCCTCTC  
ATGTGTAATTCTCCAAGCAACAGTAATGCCAATTGTGAATTTTCATTGAAAAACATCAGTGA  
CATTCATCCAGAATCCTTCAACTTGCAGTGGTTTTTCAATGACTCTTGTGCACCTCCTACTG  
GTTTCAATAAACCACAGTAACGACACCATGGCGAGTGGCTGGAGAGCÂCTAGTTTCCAC  
TTCGATTCTGAAGAAAACAAACATAGGCTTATCCACTTCTCAGTATTTTTAGGTCTATTGCT  
TGTTGGAATTCTGGAGGTCCTGTTTGGGCTCAGTCAGATAGTCATCGGTTTCCTTGGCTGTC  
TGTGTGGAGTCTCTAAGCGAAGAAGTCAAATTGTGTAGTTTAATGGGAATAAAATGTAAGTA  
TCAGTAGTTTGAAAAAAAAAAAA



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**FIGURE 176**

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA  
IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA  
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFHDSEENKHRL  
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

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**FIGURE 177**

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGAGGCT  
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT  
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC  
CAAGTTGCCAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG  
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAATTAGTGAA  
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC  
CTGATCTTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

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**FIGURE 178**

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV  
KHCTDQISFKKRLSLKKSWWK

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**FIGURE 179**

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGG  
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG  
GAGCAGATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCTCTCCCCCTGCAGCCCTGCCCCCTC  
GAACTGTGACATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGG  
AAGCCAATGACCCATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAG  
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGG  
CAAATGCAAATACAAGAGCAGCCAGAAGCAGCACAGTCCTGTACCTGAGAAGGCCATCCCAC  
TCATCACTCCAGGCTCTGCCACTACTTGCTTGAGACACAGGACTGGCCTCCAGGGATGGCCTGA  
AGCCTAACACTGGCCCCCAGCACCTCCTCCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTC  
TCTCCAAGGGCAGGCTGTTAGGCCCTTTCTGATCAGGAGGCTTCTTTATGAATTAAACTCG  
CCCCACCACCCCTCA

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**FIGURE 180**

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAGIAAVLSGKCK  
YKSSQKQHSPVPEKAIPLITPGSATTC

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**FIGURE 181**

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGGATGTCGCTGCTGAGCCTGCCC  
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC  
CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACCTGCCGCCGGCTCC  
AGTGTTTCCACAGCCCCCAAACGGAACCTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT  
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTGGCCACCTATTCCCAGGGCTTTACGGT  
ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA  
CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCCCTGAAGCCCTGG  
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC  
GCCCCCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAAACA  
TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG  
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG  
TCAGGAGAGGCCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGTAGAGAAAA  
GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGGCGGCGC  
TTCCACAGGGCCTGCCGCCTGGTGCATGACTTCACAGACGCTGTCATCCGGGAGCGGCGTCG  
CACCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG  
ATTTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT  
ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC  
CTGGGTCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC  
AAGAGCTTCTGAAGGACCGCGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC  
TTCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG  
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC  
TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC  
CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTCACCTCTGGCTTTTATTCTTTCTC  
CGCAGGGCCCCAGGAACATGCATCGGGCAGGCGTTCGCCATGGCGGAGATGAAAGTGGTCCTGG  
CGTTGATGCTGCTGCACTTCCGGTTCCTGCCAGACCACACTGAGCCCCGAGGAAGCTGGAA  
TTGATCATGCGCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCCTGAATGTAGGCTTGCA  
GTGACTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAA

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**FIGURE 182**

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPPKRNWFWG  
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF  
IRFLKPWLGEIGILLSGGDKWSRHRRLTPAFHFNILKSYITIFNKSANIMLDKWQHLLASEGS  
SRLDMEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY  
LSHDGRRFHRACRLVHDFTDAVIRERRRTLPTQGIDDFKDKAKSKTLDFIDVLLLSKDEG  
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEW  
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW  
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT  
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

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**FIGURE 183**

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATCATGTATAAGCTGGCCTCCTGC  
TGTTTGCTTTTTCACAGGATTCTTAAATCCTCTCTTATCTCTTCCTCTCCTTGACTCCAGGGA  
AATATCCTTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACTCCGGAGGAGCTAGAAA  
GAGCTTCCCTTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG  
AAAGCAGACTCAAGTACCAACATTTTTTAACCCAAGAGGAAATTTGAGAAAGTTTCAGGATTT  
CTCTGGACAAGATCCTAACATTTTACTGAGTCATCTTTTGGCCAGAATCTGGAAACCATACA  
AGAAACGTGAGACTCCTGATTGCTTCTGGAAATACTGTGTCTTGAAGTGAAATAAGCATCTGT  
TAGTCAGCTCAGAAACACCCATCTTAGAATATGAAAAATAACACAATGCTTGATTTGAAAAC  
AGTGTGGAGAAAAACTAGGCAAACTACACCCTGTTTATTGTTACCTGGAAAATAAATCCTCT  
ATGTTTTGCACAAAAAAAAAAAAAAAAA



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**FIGURE 184**

MYKLASCCLLFTGFLNPLLSLPLLDREISFQLSAPHEDARLTPEELERASLLQILPEMLGA  
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

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**FIGURE 185**

GAACATTTT TAGTTCCCAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGGAT  
GGGGTTGCTGGTTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA  
CCACCTCCGCCAGGAAGTGCAGGCCCACCTGTCTGCAACCCAGCTGAGGCCATGCCCTCCCC  
AGGGACCGTCTGCAGCCTCCTGCTCCTCGGCATGCTCTGGCTGGACTTGGCCATGGCAGGCT  
CCAGCTTCCTGAGCCCTGAACACCAGAGAGTCCAGCAGAGAAAGGAGTCGAAGAAGCCACCA  
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCCCGGAAGATGGAGGTCAAGCAGA  
AGGGGCAGAGGATGAACTGGAAGTCCGGTTCAACGCCCCCTTTGATGTTGGAATCAAGCTGT  
CAGGGGTT CAGTACCAGCAGCACAGCCAGGCCCTGGGGAAGTTTCTTCAGGACATCCTCTGG  
GAAGAGGCCAAAGAGGCCCCAGCCGACAAGTGATCGCCCACAAGCCTTACTCACCTCTCTCT  
AAGTTTAGAAGCGCTCATCTGGCTTTTCGCTTGCTTCTGCAGCAACTCCCACGACTGTTGTA  
CAAGCTCAGGAGGCGAATAAATGTTCAAAGTGA

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**FIGURE 186**

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG  
GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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**FIGURE 187**

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC  
GTGAACCCCGGGGTGCTCCGCACGGACCCAGATGTCAAGAATATGAACACGTGGCTGCTGT  
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG  
CTCCTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT  
GAGTATGTCCCCCACCCTAAGCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC  
TTACACCTCTACTTGAGTATGTCCCTAACCCTGAGCCCCCACGCCTGGGGCCAGAGTCTTT  
GTCCCCCGTGTGCGCATGTGTTCAAGGTGAGCCTCTCCAGAAGTGAGATCATGGACAAAAA  
GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCCAGCAAGAAGCTGAAC  
TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCTTGAAGTAACAAGTTTAAATGTTTCTCAGA  
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT  
CCAAAAACACAAGTAGAAATTCTAACAATGAAATATATTACAGGCAGGTACCCACTAACCA  
AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC  
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT  
AACAAACACCTCCCTGCTCCTGGCACCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCG  
TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC  
ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA  
ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTGAGGCTCTGGGCTCACCTCCATCTCCAGA  
GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCAGCTCAGAATGAACACACCCACCAAGA  
GCCTCCTTGTTTATAACACAGGTTACCCTACAAACCACTGTCCCCACACAACCCTGGGGAT  
GTTTTTAAACACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCCTGAGGGTTGA  
ATTTTTTTTAAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 188**

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLDGLVHLGQLLIFHIYLSMSPTLSPRSPQGW  
VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ  
AQQEAELTPRPAGVVPGA

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**FIGURE 189**

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACCATGGCCAAG  
ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT  
ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG  
TGCCCAAGCCCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG  
GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACTGGGAGACTGGGGATGA  
CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAACTGTGGAAG  
AACCAGGGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA  
GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA  
GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTCCCTTGGGGCTTTGTGGCAAAAATCCTA  
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT  
ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACCTGAGCGCCTTTGCTG  
CTGTTTCCTCTGTCTGTGAGGTCTCCTGGGGATGGTGGCCACATGATGTATTACAAAGTC  
TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAAATTATGGCTG  
GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA  
ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCATAGTAAGAGCTTCAAGGAAAAC  
CCGAACCTGCCTACCACATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCAC  
CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG  
GAGTCGACTTCTACTCCGAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTG  
AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA  
GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG  
TCTCTTGAGCATGGTTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC  
CTAAGGGATTCTTGGGTGCCACTGCTCTCTTTTCTCTACAGCTCCATCTTGTTTCACCCAC  
CCCACATCTCACACATCCAGAATTCCTTCTTTACTGATAGTTTCTGTGCCAGGTCTCTGGGC  
TAAACCATGGAGATAAAAAGAAGAGTAAAATACACTTCCCGACCTTAAGGATCTGAAA

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**FIGURE 190**

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP  
VSLDGDNTNTSTQEVVQYNWETGDDRFSSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR  
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPLGLCGKNPMVIPGNADHLHRTSIHQL  
PPATNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSCQLGSRRLTTTCLE  
LWLGLLHGLALLHLLHGVGCHHLQHVVHQDGAGVQVQA

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**FIGURE 191**

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAGATGTGGTTACCCCTTGGTCTCCTG  
TCTTTATGTCTTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA  
GCAGCTCCTGTGGACATTGCCATCCCCCTCTGGTAGCCTTCAGAGCAAACAGGACAACCTATG  
TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT  
GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG  
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAATCTTGCCTGCCCTATTCTCCTCCCAA  
GTCTGTTCTCTTATTGTCAACCTCAGCACAACAGGCTGGCGCCAATGGCATTACAGAGAAAG  
CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT  
AGCCACCTCCCTGTCTAGCCAGTATTAACATGTCCCCCTTCCCCCTGCCCGCCGTAGATTGAG  
GACATTCGCCCCCTGTGTGCCACCAAACCAGGACTTTCCCCTTGGCTTGGCATCCCTGGCTCT  
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT  
ATGGCGATGGCCATGATGTTACAATCCCCTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA  
GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCTGAGGAAAAACCAA  
GGGAAGCAACAGGAACCTTCTGCAACTGGTTTTTATCGGAAAGATCATCCTGCCTGCAGATGC  
TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA  
ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAAACTCTTTATTACTTTGGG  
AAGTCACTCAGCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG  
AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC  
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA



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**FIGURE 192**

MWLPLGLLSLCLSPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQSGME  
HRNHLCFCDLYDRATSPPLKCSLL

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**FIGURE 193**

GTAGCGCGTCTTGGGTCTCCCGGCTGCCGCTGCTGCCGCCGCCGCTCGGGTCTGGAGCCAGGAGCGACGTCA  
CCGCCATGGCAGGCATCAAAGCTTTGATTAGTTTGTCTTTGGAGGAGCAATCGGACTGATGTTTTTGATGCTT  
GGATGTGCCCTTCCAATATACAACAAATACTGGCCCCCTTTGTTCTATTTTTTACATCCTTTCACCTATTCC  
ATACTGCATAGCAAGAAGATTAGTGGATGATACAGATGCTATGAGTAACGCTTGTAAGGAACTTGCCATCTTTC  
TTACAACGGGCATTGTCGTGTCAGCTTTTGGACTCCCTATTGTATTTGCCAGAGCACATCTGATTGAGTGGGGA  
GCTTGTGCACTTGTCTCACAGGAAACACAGTCATCTTGAACATACTAGGCTTTTTCTTGGTCTTTGGAAG  
CAATGACGACTTCAGCTGGCAGCAGTGGTGAAAAGAAATTACTGAACTATTGTCAAATGGACTTCCTGTCATTT  
GTTGGCCATTACGCACACAGGAGATGGGGCAGTTAATGCTGAATGGTATAGCAAGCCTCTTGGGGGTATTTTA  
GGTGCTCCCTTCTCACTTTTATTGTAAGCATACTATTTTCACAGAGACTTGCTGAAGGATTTAAAGGATTTTCT  
CTTTTGAAAAGCTTGACTGATTTTCACACTTATCTATAGTATGCTTTTGTGGTGTCTGCTGAATTTAAATAT  
TTATGTGTTTTCTGTTAGGTGATTTTTTTTGAATCAATATGCAATGTTAAACACTTTTTTAATGTAATCA  
TTTGCATTGGTTAGGAATTCAGAATTCGCCGGCTCTATTACTGGTCAAGTACATCTTTCTCTAAAATTATT  
TAGCCTCCATTATTACAAAAAATTATAAAAAATAAGTTTTCACTCAGTCAGGATGACATCACTCCCAATGTTATG  
CAGACATACAGACGGTTGGCATACTGTTATAGACTGTATACTCAGTGCAAATATAGCTGCATTATACCTCAGAG  
GGGCAAGTGTTAATGCCCATGCCCTCCGTTAAGGGTGTGGTGGTTTACTGGTAGACAGATGTTTGTGGATTG  
AAAAATTATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTTCAATTGTTAGAAGAATTTATGTTAAACTTTA  
AGGTAAGGGTGTA AAAACATTTTTGAGATAAGGTTTTATTTATGTTTATTATTGTTAGAGTGAGTTGCAATGT  
GGGAAGAAATGACATTGAAATCCAGTTTTTGAATCCTGTTTCTATTTATAAGTGAATTTGTGATCTCCTATC  
AACCTTCATGTTTTACCCTGTTAAATGGACATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTTGC  
ATCATATATGCCAGAAAACCTTCCTCTGCTTCCTCCTTTTGACTTATTTGGTATGTTGTATATATTACATAAAA  
TAACTTTTCAAATATAGTTTAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTACATT  
CAGAGTGCCCCCTCCCCTGCAAGGCCTTGCCATGATTAACAAGTAACCTGTTAGTCTTACAGATAATTCATGCA  
TTAACAGTTTAAGATTTAGACCATGGTAATAGTAGTTCTTATCTCTAAGGTTATATCATATGTAATTTAAAAG  
TATTTTAAGACAAGTTTCCTGTATACCTCTGAAGTGTTTTGATTTTGAAGTTCATCATGATAGATCTGCTGTTT  
CCTTATAAAAGGCATTTGTTGTGTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACAT  
ACCTGACCAAAAAATTCAGTAACCAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAGGA  
CTTTTTTCAGGAGTGGGTTATAAAAACATTCAAGTTGGTCTGACAGTATTTTGTTAAGGATATTTGTTTGTATG  
TTTATTCAGTATACTTACATAAAAATTTTTCGCCATCAGCCAAAACCTCAGTAATCATGACAGCTGTCTGTTGT  
TTTATGAAGTTTATTTCTCAAGAAAATGGGAATAAATTTGGGATTTGTTTCTGCTTTTACTAAAGATGCCTAA  
AGCCACAGGTTTTATTGCCTAACTTAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCG  
GCGTGTGGCTGGAGCCTTCCCAGTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTTCAAGATTTCAGAGGAA  
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACCTCTTGTGCTTGTGATCTACTGGACTTT  
TTTTTTGCAGGAAGTGCAATCTCTGGTCCTTCCCTATTTTCTGTTCTGGATGTCAGTGCAGTGCAGTGCAGTGC  
TTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGCGTATTATTTCTATATACTAATTGCATTGGCAGCATT  
GTGCTTTGACCTTGATACTAGCTTGACATAGTGCTGTCTGATTTCTAGGCTAGTTACTTGAGATATGAAT  
TTCCATAGAATATGCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACCTTTTGATGATGAAACAATAA  
AGATTTTAAATATCTATTTTAAAAA

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**FIGURE 194**

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM  
SNACKELAIFLT TGIVVSAFGLPIVFARAH LIEWGACALVLTGNTVIFATILGFFLVFGSND  
DFSWQQW

**FIGURE 195**

[illegible]

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**FIGURE 196**

MDFLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH  
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNNHICSVQGDAFQKLRRVKELTLSSNQ  
ITQLPNTTFRPMPNLRSDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRI FQDCRS  
LKFLDIGYNQLKSLARNSFAGLFKLTEHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIV  
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLSIT  
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGA EPTSG  
HLLSAVTNRSDLGPPASSATT LADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA  
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH  
IEGALVIINEYGSCTCHQQPARECEV

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**FIGURE 197**

GTGCAAGGAGCCGAGGCGAGATGGGCGTCCTGGGCCGGGTCCTGCTGTGGCTGCAGCTCTGC  
GCACTGACCCAGGCGGTCTCCAAACTCTGGGTCCCCAACACGGACTTCGACGTCGCAGCCAA  
CTGGAGCCAGAACCGGACCCCGTGCGCCGGCGGCGCCGTTGAGTTCCCGGCGGACAAGATGG  
TGTCAGTCCTGGTGCAAGAAGGTCACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGGAA  
CTCGTCCTGGCTTCAGGAGCCGGATTTCGGCGTCTCAGACGTGGGCTCGCACCTGGACTGTGG  
CGCGGGCGAACCTGCCGTCTTCCGCGACTCTGACCGCTTCTCCTGGCATGACCCGCACCTGT  
GGCGCTCTGGGGACGAGGCACCTGGCCTCTTCTTCGTGGACGCCGAGCGCGTGCCCTGCCGC  
CACGACGACGTCTTCTTTCCGCCTAGTGCCTCCTTCCGCGTGGGGCTCGGCCCTGGCGCTAG  
CCCCGTGCGTGTCGCGAGCATCTCGGCTCTGGGCCGGACGTTACGCGCGACGAGGACCTGG  
CTGTTTTCTGCGTCCCGCGCGGGCCGCCTACGCTTCCACGGGCCGGGCGCGCTTCAGCGTG  
GGCCCCGAGGACTGCGCGGACCCGTGCGGCTGCGTCTGCGGCAACGCGGAGGCGCAGCCGTG  
GATCTGCGCGGCCCTGCTCCAGCCCCCT

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**FIGURE 198**

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE  
GHAVSDMLLPLDGELVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRS GDEA  
PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPGASPVRVRSISALGRTFTTRDEDLAVFLASR  
AGRLRFHGPGALSVGPEDCADPSGCVCGNAEAQPWICAALLQP

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FIGURE 199

[illegible]



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**FIGURE 200**

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP  
FARDAVKKCFVCLA

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**FIGURE 201**

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCCTCCAGTCACCCCTCCCGCCGTTACCCGCGGCGCGC  
CCGAGGGAGTCTCCTCCAGACCCCTCCCTCCCGTTGCTCCAACTAATACGGACTGAACGGATCGCTGCGAGGGT  
GGGAGAGAAAATTAGGGGGAGAAAAGGACAGAGAGAGCAACTACCATCCATAGCCAGATAGATTATCTTACACTG  
AACTGATCAAGTACTTTGAAAATGACTTCGAAATTTATCTTGGTGTCTTCATACTTGCTGCACTGAGTCTTTTC  
AACCACCTTTTCTCTCCAAGTAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACT  
TATATAAAGTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGTTACTAATGTT  
TTTATTACAAAACCTACCTTAACCATTTACTTTGGTAAGTGGCCTCTTTGCAGAGAATCATGGGATTGTTGC  
AAATGATATGTTTGATCCTATTTCGGAACAAATCTTTCTCCTTGGATCACATGAATATTTATGATTCCAAGTTTT  
GGGAAGAAGCGACACCAATATGGATCACAACCCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGA  
ACAGATGTAAAAATACATAAGCGCTTTCCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAG  
AGTTGCCAAAATTGTTGAATGGTTTACGTCAAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGAAGACCTG  
ATGACATGGGCCACCATTGTTGGGACCTGACAGTCCGCTCATGGGGCTGTCTTTTCAGATATTGACAAGAAGTTA  
GGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAACACTCTGAACCTAATCATCACAAAGTATCATGG  
AATGACGCAGTGTCTGAGGAAAGGTTAATAGAACTTGACCAGTACCTGGATAAAGACCACTATACCCTGATTG  
ATCAATCTCCAGTAGCAGCCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCAGCT  
CATCCTAATCTTACTGTTTACAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACTCGAATTCA  
ACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATGACTTTCTGTTAGGCAACC  
ACGGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTAGCCCATGGTCTCCTGCCTTCAGAAAGAATTTTC  
TCAAAAGAAGCCATGAAGTCCACAGATTTGTACCCACTACTATGCCACCTCCTCAATATCACTGCCATGCCACA  
CAATGGATCATTCTGGAATGTCCAGGATCTGCTCAATTACAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTA  
CTATACTCCTCCCTGGTAGTGTAAACCAGCAGAATATGACCAAGAGGGGTATACCCCTTATTTATAGGGGGTC  
TCTCTTGGCAGCATTATAGTGATTGTATTTTTTTGTAATTTTCATTAAGCATTAAATTCACAGTCAAATACCTGC  
CTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCCCTAATGTTACTTTGAAGTGGATTGTCATA  
TTGAAGTGGAGATTCCATAATTATGTGAGTGTAAAGGTTTCAAATCTGGGAAACCAGTTCCAAACATCTGC  
AGAAACCATTAAGCAGTTACATATTTAGGTATACACACACACACACACACATACACACACACGGACCAAA  
ATACTTACACCTGCAAAGGAATAAAGATGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATAAG  
ATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATATTTAGCAACTTTGCACTATGTAAAGTACCTTATAT  
ATTGCACTTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCACTTTATGGACAGTTATGTCTTATAAC  
TTGATTGAAAATGACAACCTTTTGCACCCATGTACAGAATACTTGTACGCATTGTTCAAACCTGAAGGAAATT  
TCTAATAATCCCGAATAATGAACATAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGA  
AAATTAATGTGATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT  
TTCTTGCTTATTTCTTCCAGAGAACGTGGTTCATTTATTTTCCCTCAAAGAGAGTCAAATACTGACAG  
ATTCGTTCTAAATATATTGTTTCTGTATATAAATTATTGTGATTTCTGATGAGTCATATTACTGTGATTTTCA  
TAATAATGAAGACACCATGAATATACTTTTCTTCTATATAGTTCAGCAATGGCCTGAATAGAAGCAACCAGGCA  
CCATCTCAGCAATGTTTTCTTGTGTTGTAATTTTGCTCCTTTGAAATTAATCACTATTAAATTACATTAA  
AAATCAAATTGGATAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 202**

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK  
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW  
ITNQ RAGHTSGAAMWPGTDVKIHKRFP THYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY  
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER  
LIELDQYLDKDHYTLDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN  
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD  
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF  
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domain:**

amino acids 429-452

**N-glycosylation sites:**amino acids 101-104, 158-161, 292-295, 329-332, 362-365, 369-  
372, 382-385, 389-392**Somatomedin B Domain:**

amino acids 69-85

**Sulfatase protein Region:**

amino acids 212-241

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**FIGURE 203**

GGATTTTTGTGATCCGCGATTTCGCTCCACGGGCGGGACCTTTGTAAGTGCAGGGAGGCCAG  
GACAGGCCCACCTGCGGGGCGGGAGGCAGCCGGGGTGAGGGAGGTGAAGAAACCAAGACGC  
AGAGAGGCCAAGCCCCCTTGCCTTGGGTCACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA  
CCAGATCCAGAGGCAACAGGGACATGGCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC  
AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA  
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGGAGG  
AGCAGCCACCACCCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCCTGACGTTGCC  
CCTGCCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAACTGTT  
CAGCTCCACAGGTTTCAGGTCATCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC  
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG  
GTATTCCACTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT  
ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG  
TGGTCTCATTATCCTGGACATTGTCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC  
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT  
TAAGACACGTTTCAAGACGGCAACTCTTAAGGTTAAAACAGATGAATGTACAATTGGCCGCCA  
AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCTGGACTGATGAGTTTGCTGTATC  
AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT  
CACACAGCCACCGTGAAAGTCCTGGAGTAAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAG  
CAGGCTGGCATGTTCACTGGGCTGGTGTACGACAGAGAACCTGACAGTCACTGGCCAGTTA  
TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC  
AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 204**

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYYKKWENEEEEEEEEQPPPTPV  
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFSSHRFQVIIICLVVLDALLVLAELIDL  
KIIQPDKNYYAAMVFHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILDI  
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLRLKQMNVLAAKIQHLEFS  
CSEKPLD



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**FIGURE 206**

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD  
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEEKILK  
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTVPDEFTVEERQTGMW  
WRHLVAGGGAGAVSRTCTAPLDRLKVLQMQRHASRSNNMGIVGGFTQMIREGGARSLWRGNGI  
NVLKIAPESAIKFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMAL  
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNWLQHYAVNS  
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSSLFKHILRTEGAFG  
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

**Important features:****Signal peptide:**

amino acids 1-16

**Transmembrane domain:**

amino acids 284-304, 339-360, 376-394

**Mitochondrial energy transfer proteins signature.**

amino acids 206-215, 300-309

**N-glycosylation site.**

amino acids 129-133, 169-173

**Elongation Factor-hand calcium-binding protein.**

amino acids 54-73, 85-104, 121-140

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**FIGURE 207**

GGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCAT  
GGCTTCCCTGGGGCAGATCCTCTTCTGGAGCATAATTAGCATCATCATTATTCTGGCTGGAG  
CAATTGCACTCATCATTGGCTTTGGTATTTAGGGAGACACTCCATCACAGTCACTACTGTC  
GCCTCAGCTGGGAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCAA  
ACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCA  
AAGAAGGCAAAGATGAGCTGTGCGAGCAGGATGAAATGTTGAGAGGCCGGACAGCAGTGTTT  
GCTGATCAAGTGATAGTTGGCAATGCCTCTTTCGGGCTGAAAAACGTGCAACTCACAGATGC  
TGGCACCTACAAATGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATA  
AAACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTG  
CGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCA  
GGGAGCCAACCTTCTCGGAAGTCTCCAATACCAGCTTTGAGCTGAACTCTGAGAATGTGACCA  
TGAAGGTTGTGTCTGTGCTCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAA  
AATGACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAAAAGGCGGAG  
TCACCTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGTCTCTTCTTTCTTTGCCATCAGCT  
GGGCACTTCTGCCTCTCAGCCCTTACCTGATGCTAAAATAATGTGCCTTGGCCACAAAAAG  
CATGCAAAGTCATTGTTACAACAGGGATCTACAGAACTATTTACCACCAGATATGACCTAG  
TTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCA  
AGAAACAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACAAGATAAATCTATCTTCAA  
GACATATTAGAAGTTGGGAAAATAATTCATGTGAAGTAGACAAGTGTGTTAAGAGTGATAAG  
TAAAATGCACGTGGAGACAAGTGCATCCCCAGATCTCAGGGACCTCCCCCTGCCTGTCACCT  
GGGGAGTGAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTATGTTATATGTGCTG  
TAATGTTGCTCTGAGGAAGCCCCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCA  
CAAATTAAGCTGTAGTATGTACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGG  
GGCGGCTGCATTTTAGTAATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCT  
TGGCTTCTCTTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAA  
ACAGAGCAGTCGGGGACACCGATTTTATAAATAAACTGAGCACCTTCTTTTAAACAAAAAA  
AA



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**FIGURE 208**

MASLGQILFWSIISIIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI  
KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTD  
AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD  
QGANFSEVSNTSFELNSENVTMKVSVLYNVTINNTYSCMIENDIAKATGDIKVTSESEIKRR  
SHLQLLSKASLCVSSFFAISWALLPLSPYLMLK

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FIGURE 209

[illegible]

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**FIGURE 210**

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMPFL  
LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS  
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

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**FIGURE 211**

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG  
GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTCGAAAAGATTCCGCAATAAACT  
TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT  
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCA**ATGA**AGGGCATCCTCG  
TTGCTGGTATCACTGCAGTGCTTGTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT  
TCATGGGAAAAATCCTGTGTCAACAGCATTGCCTCTGAATGTCCCTCACATGCCAACACCAG  
CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATAACCAGAATATGT  
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT  
GCTGAAGAACACTTTTCATTTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG  
CGATGCCCTGGACCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG  
AATCTAATGGAACCTCCTGTCTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC  
TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTC  
CAACGTCAGTAACGCCACCTGTCACTTCCCTGTCTGGTGAAAACAAGACTCTTGAGGAGTCA  
TCTTTGAAAAGTTTGAGTGTGCAAATGTAAACAGCTTAACCCCCACGTCTGCACCAACCACT  
TCCCACAACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGCCCTTGCCAGCCTCCTTCTTCG  
GGGACTGCTGCCCC**TGAG**GGTCCTGGGGCTGCACTTTGCCAGCACCCCATTTCTGCTTCTCTG  
AGGTCCAGAGCACCCCCTGCGGTGCTGACACCCTCTTCCCTGCTCTGCCCCGTTTAACTGC  
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA  
AAGCACTGGTTCATTCACTGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 212**

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR  
LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE  
CPACYESNGTSCRGKPKWCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK  
TLGGVIFRKFEKANVNSLTPTSAPTTSNHNVGSKASLYLLALASLLLRGLLP

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**FIGURE 213**

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA  
GGGCTTGCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCCATGGTCCCCGCCGCCG  
GCGCGCTGCTGTGGGTCTGCTGCTGAATCTGGGTCCCCGGGCGGCGGGGGCCCAAGGCCTG  
ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCATGACCCGCAG  
CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA  
ATGATGCCATGGCCGACGCCGACCGCTGGCTGGACCAGCGGCTGCCGAGCTCTTGCCGCC  
ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA  
GGGGGTTGTGATTAATGCCGGAAGGATAGCACCAGCAGAGAGCTTCCCAGTGCGACTCCCA  
ATACAGCGGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG  
ACTTCAAGCCTGCCGCGCTCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC  
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTCACCTCACCCACAG  
CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC  
TGCAAGTCGGGCACCATGAGCCGAGCCGGTCTGGGAAGCTGCACGGCCTTTCGGGGCGCCT  
TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGACCTATCAACAATGTC  
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT  
GCCTCTCAGAGCACCACCAGTACCAGGACCACCACTACCCCTTCCCCACCATCCACCTCAG  
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCTGCCAGCCCTGGCTTTTTGGAAACGGGTCA  
GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTACAGAGATGCAACCAATA  
GACAGAAACCAGAGGTAATGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT  
CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTGTACAGAAAAACAAACTGGAAAA  
CACAA

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**FIGURE 214**

MVPAAGALLWVLLLNLGPRAAGAQGLTQTPTMQRVSLRFGGPMTRSYRSTARTGLPRKTRI  
ILEDENDAMADADRLAGPAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL  
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP  
SPSPTAMPSPEDLRLVLPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC  
TYQQCPCNRLREECPLDTSLCDTNCASQSTTSTRTTTTPFPTIHLRSSPSLPPASPCPALA  
FWKRVIRIGLEDIWNSLSSVFTEMQPIDRNQR

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**FIGURE 215**

CCCGGGTCGACCCACGCGTCCGGGGAGAAAGGATGGCCGGCCTGGCGGCGCGGTTGGTCCTGCTAGCTGGGGCA  
GCGGCGCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGACCGCGACTGCGTACTGCACTGCGAAGAGCA  
GAACTGCTCTGGGGGCGCTCTGAATCACTTCCGCTCCCGCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCT  
GTCGGGACGACTGTAAGTATGAGTGTATGTGGGTACCGTTGGGCTCTACCTCCAGGAAGGTCACAAAGTGCCCT  
CAGTTCATGGCAAGTGGCCCTTCTCCGGTTCTGTTCTTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTTCT  
CAATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCCATGTACCACA  
CCTGTGTGGCCTTCGCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGTCTTCCACACCAGGGACACTGAC  
CTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCATCCTACACTCAATCTACCTGTGCTGCGTCAGGAC  
CGTGGGGCTGCAGACCCAGCTGTGGTCAGTGCCTTCCGGGCTCCTGCTGCTCATGCTGACCGTGACAGTCT  
CCTACCTGAGCCTCATCCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTG  
GTGTGGTGGCTGGCCTGGTGCCTGTGGAACAGCGGCGGCTGCCTCACGTGCGCAAGTGCGTGGTGGTGGTCTT  
GCTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCCACCGCTCTTCTGGGTCTGGATGCCCATGCCA  
TCTGGCACATCAGCACCATCCCTGTCCACGTCTCTTTTTAGCTTTCTGGAAGATGACAGCCTGTACCTGCTG  
AAGGAATCAGAGGACAAGTTCAAGCTGGACTGAAGACCTTGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCC  
GCCCTGCTGGCCTCCCTTCTCCCTCAACCCTTGAGATGATTTCTCTTTTCAACTTCTTGAAGTGGACATGA  
AGGATGTGGGCCCAGAATCATGTGGCCAGCCCCACCCCTGTGGCCCTCACCAGCCTTGGAGTCTGTTCTAGGG  
AAGCCTCCCAGCATCTGGGACTCGAGAGTGGGACGCCCTCTACCTCCTGGAGCTGAAGTGGGGTGGAACTGA  
GTGTGTTCTTAGCTCTACCGGAGGACAGCTGCCTGTTCTCTCCCAACAGCCTCCTCCCAATCCCCAGCTG  
CCTGGCTGGGTCTGAAGCCCTCTGTCTACCTGGGAGACCAGGGACACAGGCCTTAGGGATACAGGGGGTCCC  
CTTCTGTTACCACCCCCACCTCCTCCAGGACACCACTAGGTGGTGGTGGATGCTTGTCTTTGGCCAGCCAA  
GGTTCACGGCGATTCTCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTACCCTGACC  
GTTGCCCTAGCCAGGTTCACAGGAGGCTCACCATACTCCCTTTAGGGCCAGGGCTCCAGCAAGCCCAGGGCA  
AGGATCCTGTGCTGCTGTGTTGAGAGCCTGCCACCGTGTGTGCGGAGTGTGGGCCAGGCTGAGTGCATAGG  
TGACAGGGCCGTGAGCATGGGCTGGGTGTGTGTGAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGT  
CGGGGAAGAGGTGTGGCTTCAAAGTGTGTGTGTGCAGGGGTGGGTGTGTTAGCGTGGGTAGGGGAACGTGTG  
TGCGCGTGTGTTGGCATGTGAGATGAGTACTGCCGTGAATGTGTCCACAGTTGAGAGGTGGAGCAGGAT  
GAGGGAATCCTGTACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCAAGACGCCACCTGGGCGGACAGC  
CAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGGTGGCCCTTTGGCCGCTCCTGCAAC  
CTCACAGGGTCCCCACACAAGTGCCTCCAGAAGCAGCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGC  
TGGGGCTCTCTCCATCCTCTTTCTCCTTGCCCTTCGCATGGCTGGCCTTCCCCTCCAAAACCTCCATTCCCCT  
GCTGCCAGCCCCTTTGCCATAGCCTGATTTTGGGGAGGAGGAAGGGGCGATTTGAGGGAGAAGGGGAGAAAGCT  
TATGGCTGGGTCTGTTTCTTCCCTTCCAGAGGCTTACTGTTCCAGGTGGCCCCAGGGCAGGCAGGGGCC  
ACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGCCCTGGCATGTTCTTCCCCACAGG  
AATAGAATGGAGGGAGCTCCAGAACTTTCCATCCCAAAGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTTG  
CTCTGCCCTGACCCCTTGTCCCTCTTTGAGGGAGGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTG  
GCCTGCGCTAGCTTCTTTGATACTGAAACTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAA  
TTCCAAGCCTCAAAAAAAAAAAAAAAAAA



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**FIGURE 216**

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW  
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSSRFLFFQEPASAVASFLNGLASLVMLCR  
YRTFVPASSPMYHTCVAFAWVSLNAFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR  
TVGLQHPAVVSAFRALLLMLTVHVSYSLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR  
RLPHVRKCVVVVLLLQGLSLLELLDFPPLFWVLDAAHAIWHISTIPVHVLFFSFLEDDSLYLL  
KESEDKFKLD

**Important features:****Signal peptide:**

amino acids 1-20

**Transmembrane domains:**

amino acids 105-123, 138-156, 169-185, 193-209, 221-240, 256-272

**N-glycosylation site.**

amino acids 40-44

**N-myristoylation site.**

amino acids 43-49

**CUB domain proteins profile.**

amino acids 285-302

**Amiloride-sensitive sodium channels proteins.**

amino acids 162-186

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**FIGURE 217**

[illegible]

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**FIGURE 218**

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEL  
DAEVLEVFPHTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTN  
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV  
RLINKFNSSSSSLEEKIAALFDLEYVHQM DNAQD LLSFGGLQVVINGLNSTEPLVKEYAAF  
VLGA AFSSNP KVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL  
GGLQVLR TLVQ EKGTEVLAVRVV TLLYDLVTEKMF AEEEAELTQEMSPEKLQQYRQVHLLPG  
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS  
LELQDGEDEGYFQELLGSVNSLLKELR

**Important features:****Signal peptide:**

amino acids 1-29

**Hypothetical YJL126w/YLR351c/yhcX family protein.**

amino acids 364-373

**N-glycosylation site.**

amino acids 193-197, 236-240

**N-myristoylation site.**

amino acids 15-21, 19-25, 234-240, 251-257, 402-408, 451-457

**Homologous region SLS1 protein.**

amino acids 68-340

FIGURE 219

[illegible]

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**FIGURE 220**

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIIILVAGAFFWLVSLLLASVWVFILVHVTDR  
SDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS  
FGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAAIILLHTFWGVVFFDACERRR  
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLCKD

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**FIGURE 221**

AAGCTGGTTTAAGGAAGCAGAGGAGGGTTAGATTCGTTGAGTGAGGACGGAAGATCAACCCA  
TTTCCATTCCGCCAGATGGCCTATGTTTCTGGTCTCTCCCTTCGGNATCATCAGTGGTGTNT  
TNTCTGTTATCAATATTTTGGCTGATGCANTTGGGCCAGGTGTGGTTGGGATCCATGGAGAC  
TCACCCTATTANTTCCTGANTTCAGCCTTTNTGACAGCAGCCATTATCCTGCTC

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**FIGURE 222**

GACCGACCGTTCAGATGCCCCGGTTCCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG  
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG  
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN  
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTGGNTGATGCAN  
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCTATTAATTCCTGAATTCAGCCTTT  
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTGTTTTTTGATGCCTGTGA  
GAGGAG

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**FIGURE 223**

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCGGTTTCCCCCCTTCCCTTTCCCCG  
GGGTCTGGGGTGACATTGCACGGGCCCCCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCC  
CCAGNTGGNGCGCCCTTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCTTCCCACNTG  
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGCCCGGCCTTCG  
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA  
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGAC  
CGACCGGTCAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTTGGTGCTGCTGTCTCTGTCC  
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA  
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG  
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTTG  
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC



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**FIGURE 224**

GTAAAAGAAAGTGGCCGGACCTTCATTGGGGTTTCGGTTCCCCCCTTTCCCNNTTCCCCGGGG  
TCTGGGGGTGACATTGCACCGCGCCCNTCGTGGGGTCGCGTTGCCACCCCACGCGGACTCCC  
CAGNTGGCGCGCCCCCTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCTTCCACCTGA  
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTCGCGTTCTGGGCCCGGCCTTC  
GCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGC  
ATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGA  
CCGACCGGTGAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTC  
CTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT  
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG  
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTGGCTGATGCACTT  
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

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**FIGURE 225**

GCCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCGGTGCCAGAGCCCAGGAGGAGGCAG  
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCACCCCC  
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAGGAGAGG  
TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCT  
AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCGT  
CCTTGTGGTTTCCTCTCTACCTGGGGAAATAAGGTGCAGCGGCCATGGCTACAGCAAGACCCC  
CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTACAGAGCATGTT  
CTCGCCAACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA  
GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCGGTGCGATGACAGCAGCAGCCGCATCATCA  
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC  
CAGCTCTACTGCGGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCACTGCAG  
GAAGAAAGTTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC  
AGCAGATGTTCCAGGGGGTCAAATCCATCCCCACCCCTGGCTACTCCCACCCCTGGCCACTCT  
AACGACCTCATGCTCATCAAACCTGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCAT  
CAACGTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGACAA  
CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT  
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA  
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCC  
TGCAGGGACTCGTGTCTCTGGGGAGATTACCCCTGTGCCCGGCCCAACAGACCGGGTGTCTAC  
ACGAACCTCTGCAAGTTACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCAT  
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTTCAG  
ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTTCATCTCTCCAGCCCCTGACCCCATGTCT  
CCTGGACTCAGGGTCTGCTTCCCCACATTGGGGTGACCGTGTCTCTCTAGTTGAACCCCTGG  
GAACAATTTCCAAAACCTGTCCAGGGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTTCAT  
CCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA  
CTGAGAAGTGGAATAAAAAA

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**FIGURE 226**

MATARPPWMWVLCALITALLGVTEHVLANNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDD  
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS  
PVYESGQQMFQGVKSI PHPGYSHPGHSNDLMLIKLNRIRPTKDVRPINVSSHCP SAGTKCL  
VSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGR DSCQGDSGGP  
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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**FIGURE 227**

**ATGGTCAACGACCGGTGGAAGACCATGGGCGGCGCTGCCCAACTTGAGGACCGGCCGCGCGA**  
CAAGCCGCGAGCGGCCGAGCTGCGGCTACGTGCTGTGCACCGTGCTGCTGGCCCTGGCTGTGC  
TGCTGGCTGTAGCTGTACCGGTGCCGTGCTCTTCTGAACCACGCCACGCGCCGGGCACG  
GCGCCCCACCTGTCTGTCAGCACTGGGGCTGCCAGCGCCAACAGCGCCCTGGTCACTGTGGA  
AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCGACCTACCGACA  
GCTTCGCACGCCTGGAGAGCGCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC  
CAGCCACGGCTGGTGGGCGACAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC  
CCGGCTGCTGGCCGAGCCTCAGAGCTGCAGACGGAGTGCATGGGGCTGCGGAAGGGGCATG  
GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCTCATCCAGCTCTC  
TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACCTCCGTCAGCGACATCCTGGATGCCCT  
GCAGAGGGACCGGGGGCTGGGCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCC  
GGGGAACCCGGCCCCGGGGCTGTGCCACTGGCTCCCCGGCCCCGAGACTGTCTGGACGTCCTC  
CTAAGCGGACAGCAGGACGATGGCGTCTACTCTGTCTTTCCACCCACTACCCGGCCGGCTT  
CCAGGTGTACTGTGACATGCGCACGGACGGCGGGCTGGACGGTGTTCAGCGCCGGGAGG  
ACGGCTCCGTGAACCTTCTTCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC  
GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT  
GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG  
TGGGCTTGTCTCCGTGGACCCTGAGGAAGACGGGTACCCGCTCACCCTGGCTGACTATTCC  
GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGGCATGAGGTTACCCACCAAGGACCGTGA  
CAGCGACCATTAGAGAACAACCTGTGCCGCTTCTACCGCGGTGCCTGGTGGTACCGCAACT  
GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC  
GTGGAGTGGTCTCTGGACCGGCTGGCAGTACTCACTCAAGTTCTCTGAGATGAAGATCCG  
GCCGGTCCGGGAGGACCGCT**TAG**ACTGGTGACCTTGTCTTGGCCCTGCTGGTCCCTGTCTCG  
CCCATCCCCGACCCACCTCACTCTTTCTGATGTTCTTCCACCCACCTGTGCTGGCGGAC  
CCACTCTCCAGTAGGGAGGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT  
CACACATCGCCTTCTCGCCGTCCCCACCCCTCCATTTGGCAGCTCACTGATCTCTTGCCCTC  
TGCTGATGGGGCTGGCAAACCTTGACGACCCCAACTCCTGCCTGCCCCCACTGTGACTCCGG  
GCTGTTTGCCGTCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCTCTGCCCTGCC  
GGCCAAATACCCGGCATTATGGGGACAGAGAGCAGGGGGCAGACAGCACCCCTGGAGCTC  
CTAGCAGATCGTGGGGAATGTCAGGTCTCTCTGAGGTGAGGTCTGAGGCCAGTATCCTCCAG  
CCCTCCCAATGCCAACCCCAACCCCGTTTCCCTGGTGCCAGAGAACCCACCTCTCCCCAA  
GGGCCTCAGCCTGGCTGTGGGCTGGGTGGCCCCATCCTACCAGGCCCTGAGGTGAGGATGGG  
GAGCTGCTGCCCTTGGGGACCCACGCTCCAAGGCTGAGACCAGTTCCCTGGAGGCCACCCAC  
CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCTCTTACCTGCTGTGCCCACCTGCTCTCTG  
TCTCAAATGAGGCCCAACCCATCCCCACCCAGCTCCCGGCCGTCTCCTACCTGGGGCAGC  
CGGGGCTGCCATCCCATTTCTCCTGCCTCTGGAAGGTGGGTGGGGCCCTGCACCGTGGGGCT  
GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCCTAGGCAGGGCTGGGATGAG  
GCTTGTAACCCCCACCACCAATTTCCAGGGACTCCAGGGTCCAGGGCTCCAGGGCTCCAGGAGG  
GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCCTTGCC  
ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCCGGCCGGCGAGTGGTCAAGGGACAGGGA  
CCACCTCACCGGGCAATGGGGTCCGGGGGACTGGGGCACCAGACCAGGCACCACTGGACA  
CTTTCTTGTGAATCCTCCCAACACCCAGCAGCTGTATCCCCACTCCTTGTGTGCACACA  
TGCAGAGGTGAGACCCGACGGCTCCAGGACCAGCAGCCACAAGGGCAGGGCTGGAGCCGGG  
TCCTCAGCTGTCTGCTCAGCAGCCCTGGACCCGCGTGCCTTACGTGAGGCCAGATGCAGGG  
CGGCTTTTCCAAGGCCTCCTGATGGGGGCTCCGAAAGGGCTGGAGTCAGCCTTGGGGAGCT  
GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGAGGTGGCTTCCTCCAAAGGACACCCGATGGCA  
GGTGCCTAGGGGGTGTGGGGTTCGGTTCTCCCTTCCCTCCCACTGAAGTTTGTGCTTAAAA  
AACAATAAATTTGACTTGGCACCACTGGGGGTGGTGGGAGAGGCCGTGTGACCTGGCTCTC  
TGTCCCAGTGCCACCAGGTCATCCACATGCGCAG

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**FIGURE 228**

MVNDRWKTMGGAAQLEDRPRDKPQRPSGCVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT  
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA  
QPRLVGDQEQELDLTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLLIQLL  
SESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL  
LSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRRDGSVNFFRGWDAYRDGFGRLT  
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAAYARYGSFGVGLFSVDPEEDGYPLTVADYS  
GTAGDSLKXSGMRFTTKDRSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASADG  
VEWSSWTGWQYSLKFSEMKIRPVREDR

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**FIGURE 229**

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT  
TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCAGGGCAATCCGACCACATTTCACTCT  
CACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG  
ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTCGGCATCCAGAGCCC  
CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC  
TTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTTCAGTACTACC  
AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATACGTCC  
CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC  
TGAAAACTCTGTCTGTAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG  
AACAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG  
GACTGTAAATATTTCTGCCTTAGTGAAACTCTACCATGCTGAAGATAAACAAACAAGAAGA  
CCTGGAATTTGCCGCTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT  
TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGATGGAACCCCTTTCACTTCTGAACTG  
TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG  
GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA  
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCGAAGGTGACTTGATTCGCC  
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT  
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG  
TTTCCTGTTTCAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA  
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCATAATGTCATCTGCCTTCTTG  
GCTTAGAGATAACTTTTAGCTCTCTTTCTTCTCAATGTCTAATATCACCTCCCTGTTTTCAT  
GTCTTCCTTACACTTGGTGGAATAAGAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC  
ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC  
AGCAAATACACAAGGAATTCTTTTTGTTTGTTCAGTTCATACTAGTCCCTTCCCAATCCAT  
CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG  
AATCTCAAATCTCAATGCCTTATAAGCATTCCTTCCTGTGTCCATTAAGACTCTGATAATTG  
TCTCCCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCATCTCCGTTTCATATCAG  
AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA  
TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAG  
GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

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**FIGURE 230**

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLL  
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE  
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS  
QSYSEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD  
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

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**FIGURE 231**

AATTTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG  
ATGATGATGGGACACCACCATGAGCCTGCATTNTCAAGCTTTTGCCACAATTCGGCATCCAG  
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTTTCAACGTGGCGACCAGTGGCCCTGACCCTG  
CTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTA  
CTACCAGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATA  
CGTCCCAAGAGTTGCAATTTNTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTNTGCAGCAT  
GTGGCTGAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGGAACCTTTGAAGGAGGGCAA  
AGTNTCCTCATNTACTATACACACACCACTTCCC



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**FIGURE 232**

GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGGCGGGCTC  
CGGGGATTCGGCTCGGGCCGCTGGCTCTGCTCTGCGGGGAGGGAGCGGGCCCCGCGGGG  
CCCGAGCCCTCCGGATCCGCCCCCTCCCCGGTCCCGCCCCCTCGGAGACTCCTCTGGCTGCT  
CTGGGGGTTCGCGGGGGCCGGGGACCCGCGGTCCGGGCGCCATGCGGGCATCGCTGCTGCTG  
TCGGTGCTGCGGCCCCGAGGGCCCCGTGGCCGTGGGCATCTCCCTGGGCTTCACCCTGAGCCT  
GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCAGGCCCGCCCCAACCTGGAGACTCTG  
AGCTGCCGCCGCGCGGCAACACCAACGCGCGCGCGGCCCAACTCGGTGCAGCCCCGGAGCG  
GAGCGCGAGAAGCCCGGGGCGGCGAAGGCGCGGGGAGAATTGGGAGCCGCGCGTCTTGCC  
CTACCACCCTGCACAGCCCCGGCCAGGCCGCCAAAAAGGCCGTGAGGACCCGCTACATCAGCA  
CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC  
ACGCTGGGCGTGGCCGTGAACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC  
GGGCGCACGGGGCCGCCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC  
CCATTGGACACCTGCACCTGGCGCTGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC  
TGGTTCTTCTTGGTGCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG  
CCACCTCAGCCTGGCCTCCGCCGCCACCTGTACCTGGGCCGGCCCCAGGACTTCATCGGCG  
GAGAGCCCACCCCCGGCCGCTACTGCCACGAGGCTTTGGGGTCTGCTGCTGCGCGCATGCTG  
CTGCAACAACCTGCGCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGC GCGCCCTGA  
CGAGTGGCTGGGTGCTGCAATTCTCGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG  
GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGACAGGAGGGGACCCTCAT  
TTCCGAAGTGCCCTGACAGCCCACCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA  
AGCTTTGCCCCGAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA  
TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCGTGGGTATT  
CCAGCACCATCCCGCCCGGCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA  
GCACGCTTTCTCTGCGCCGATGGCTCACCCCGTGCCCACTGCGTGGGGCTGACCGGGCTG  
ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCAACCGCCCTG  
CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCGGGGTATGGA  
ATACACGCTGGACTTGACAGCTGGAGGCACTGACCCCCCAGGGAGGCCGCGGCCCTCACTC  
GCCGAGTGACAGCTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCTGTGCCCTATGTCACT  
GAGGCCCTCACGTCTCACTGTGCTGCTGCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCCTGG  
CTTCTTGAGGGCCTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC  
TGCTGCTACTGTATGAGCCGCGCCAGGCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT  
GTCAAGGCCCACGTGGCAGAGCTGGAGCGGCGTTTCCCCGGTGCCCGGGTGCCATGGCTCAG  
TGTGCAGACAGCCGCACCCTCACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC  
TGGACACACTGTTCTCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCCTGAACCGC  
TGCCGCATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA  
CCCAGGTGTGGCCCCACCACAAGGGCCTGGGCCCCCAGAGCTGGGCCGTGACACTGGCCGCT  
TTGATCGCCAGGCAGCCAGCGAGGCCTGCTTCTACAACCTCCGACTACGTGGCAGCCCCGTGGG  
CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGAGCTGCTGGAGAGCCTGGATGTGTACGAGCT  
GTTCTTCCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGCGCTGCTGCAGCGCT  
ACCGGGCCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCTCCAGAGC  
GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG  
CAACAGCACCTTGACCCCACCCTGTCCCCGTGGGCCGTGGCATGGCCACACCCACCCCACTT  
CTCCCCAAAACCAGAGCCACCTGCCAGCCTCGTGGGCAGGGCTGGCCGTAGCCAGACCCC  
AAGCTGGCCCCACTGGTCCCCCTCTTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG  
GGACGTGCCCCCAGAGCCACCCACTTCTCATCCAAACCCAGTTTCCCTGCCCCCTGACGCT  
GCTGATTGCGGCTGTGGCCTCCACGATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC  
CTCTGGGCCCTGGGGGCTGGGCTGTAGAAGAGTTGTTGGGGAAGGAGGAGCTGAGGAGGGG  
GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA  
AGTGTGGAAAAA

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**FIGURE 233**

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP  
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAACKAVRTRYISTELGIRQLLVAVL  
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPIGHLHLALRHLE  
QHGDDEFDWFLLVPDTTYTEAHGLARLTGHLASASAHLYLGRPQDFIGGEPTPGRYCHGGFG  
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDTGCVGCTGDHEGVHYSHLELSPGEP  
VQEGDPHFERSALTAHPVRDPVHMYQLHKAFARAELEPTYQEIQELQWEIQNTSHLAVDGDRA  
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTAEELN  
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI  
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQ RVA  
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVL  
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQGGPPELGRDTGRFDRQAASEACFYNS  
DYVAARGRLAAASEQEEELLESLDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDL  
YHRCLQSVLEGLGSRTQLAMLLFEQE QGNST

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**FIGURE 234**

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT  
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT  
AGCTATTAGCCAATTTCGGCAGGGCCCGCTTTTTAGAAAGCTTGATTTCCTTTGAAGATGAAAG  
ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA  
CTGTATCCACCCAAATGTCACCGATTTCTTCCTATGCAGGAAATGAGCAGACCCATCAATAA  
GAAATTTCTCAGCCTGGCCGAAAATGGTTGGCCCCACGAAGCCACGACAACCTGGAGGCCAAAG  
AGGGTTGCTCAACGCCCCGCCTCATTGGA AAACCAAATCAGATCTGGGACCTATATAGCGTG  
GCGGAGGCGGGGCGATGATTGTGCGGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT  
TTCCCCGCCCCTGAGACCCTGCAGCACCATCTGTCAATGGCGGCTGGGCTGTTTGGTTTGAGC  
GCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGCTCCCGGCCGCCCGCGTCCGCTGGGA  
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC  
CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACCTTGTATGAGAAGAACCCA  
GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT  
CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA  
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC  
CTTCCCATCATGGAATCCAACCTGCTTCGACCCAGCAAGATCCAGCTGCCAGAGGATGAGTG  
ACCAGTTGCTAAGTGGGGCTCAAGAAGCACCGCCTTCCCCACCCCCTGCCTGCCATTCTGAC  
CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

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**FIGURE 235**

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE  
DENLYEKNPD SHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER  
LVKYREANGLPIMESNCFDPSKIQLPEDE

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**FIGURE 236**

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGC  
TCCCGGCCGCCCGCGTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT  
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA  
CGAAACTTGTATGAGAAGAACCCAGACTCCCATGGTTATGACAAGGACCCCGTTTTGGACG  
TCTGGAACATGCGACTTGTCTTCTTCTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC  
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT  
TGTGAAATACCGAGAGGCCAATGGCCTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCA  
AGATCCAG

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**FIGURE 237**

GCGGCGGCT**ATG**CCGCTTGCTCTGCTCGTCCTGTTGCTCCTGGGGCCCCGGCGGCTGGTGCCT  
TGCAGAACCCCCACGCGACAGCCTGCGGGAGGAACTTGTCATCACCCCGCTGCCTTCCGGGG  
ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTTCGGAGCTTCAGCGGGAAGGAGTG  
TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA  
GCTGCACCTGTCAATCACACAAGGCTTTTGGAGGACCCGATACTGGGGGCCACCCTTCCTGC  
AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA  
TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA  
CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG  
ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC  
CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA  
TCGCTTGTTCCACACCAGCTACCACTCCCAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG  
CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC  
ATCACGGGGCAGGGAAAGAAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCCTCACGGA  
GCCCTGCCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACTACAACCAGGACA  
ACGAGACATTAGAGGTGCACCCACCCCCGACCACTACATATCAGGACGTCATCCTAGGCCT  
CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACCTCTCGAAACCT  
CAACATCCAGCTCAAGTGGAAGAGACCCCCAGAGAATGAGGCCCCCCCCAGTGCCCTTCCTGC  
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC  
AACACCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG  
GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC  
ACTACCAGCCTGCCCAGGACCGGTGCAACCCACCTCCTGGAGATGCTGATTCAGCTGCCG  
GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA  
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCTCAGCGCCCTTGTGCCCA  
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCCTCTTCAACAGCCTGTTCCCA  
GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC  
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT  
GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT  
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCGCCCGAGGTGTCCCCCACTCT**GATT**  
CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCCAAGGGCTGTT  
TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTACAGGC  
CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTGGAATTTGAATTAA  
CTTAGAAATTCATTTCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA  
AGTGGTCGGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACACAGAAAGGTC  
GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGA  
TGGAGTTTACTGTTTGTGGAATAAAAACGGCTGTTTCCGTGGAAAAAAAAAAAA

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**FIGURE 238**

MPLALLVLLLLGPGGWCLAEPDRSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY  
RLFPKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVTDVDSWK  
ELSNVLSGIFCASLNFIDSTNTVTPTASFPLGLANDTDHYFLRYAVLPREVVCTENLTPWK  
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCNRARCTSSWELRQTLVVFDAFITG  
QGKKDWSLFRMFSRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT  
YAIYDLLDTAMINNSRNLNIQLKWKRPPEAPPVPFLHAQRYVSGYGLQKGLSTLLYNTH  
PYRAFPVLLLDTPWYLRLYVHTLTITSGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS  
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAKPVDWEESPLFNSLFPVSD  
GSNYFVRLYTEPLLNLPTPDFSMPYNVICLTCTVVAVCYGSFYNLLTRTFHIEEPRTGGLA  
KRLANLIRRARGVPPL

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**FIGURE 239**

CAACATGGGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTTGTGACCCTGGTGG  
CTGTGGAAGGAGTTAAAGAGGGTATAGAGAAAGCAGGGGTTTGCCCAGCTGACAACGTACGC  
TGCTTCAAGTCCGATCCTCCCCAGTGTCACACAGACCAGGACTGTCTGGGGGAAAGGAAGTG  
TTGTTACCTGCACTGTGGCTTCAAGTGTGTGATTCCTGTGAAGGAACTGGAAGAAGGAGGAA  
ACAAGGATGAAGATGTGTCAAGGCCATACCCTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC  
TCCTCCTCTACCAGGTGTCCTCAGAATGATGCTGGGTCTTTCTACCTCTGGGGGTCACTC  
TCACTTGGCACCTGCCCCTGAGGGTCCTGAGACTTGGAATATGGAAGAAGCAATACCCAACC  
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTTCCCCAAAAGAGGGAAGAGTCACAAAAAG  
TCCAGACCCAGGGACGGTACTTTCCCTCTCTACCTGGTGCTCCTCCCTAATGCTCATGAAT  
GGACCCCTCATGAATGAAACCAGTGCCCTTATAAGAGACCCCAAAGAGCTGCCTTGCCCTTC  
TGCAATGTGTGATCACAGCTAGAAGGCACTGTCAGAGAAGAGAACTGGTCTCACCAGATG  
CTGAATCTGCTGGTGCCTTGATCTTGGACTTCCCAGCCTCTAGAACTGTAAGAAATAAATAT  
TTGCTGTTTATAATCCAA



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**FIGURE 240**

MGSSSFLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC  
YLHCGFKCVIPVKELEECCGKDEEDVSRPYEPGWAKCPGSSSTRCPQK

**Signal sequence:**

amino acids 1-19

**N-myristoylation sites:**

amino acids 23-29, 27-33, 32-38, 102-108

**WAP-type 'four-disulfide core' domain signature:**

amino acids 49-63

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**FIGURE 241**

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG  
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC  
TCTAGAACCCGACCCACCACCATGAGGTCCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG  
CGTCCAGTGGTCCTTGCTTCTGGCTGTCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTA  
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATTAAAGAAAGGTCT  
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA  
TGCAGAGCCAGCGCCAGAGACAATGCCCTCAACACACAAACCCAGCCCAAGGCCACACCA  
CCGGAGACAGAGGAAAGGAGGCCAACAGGCACCGCCGGAGGAGCAGGACAAGGTGCCCCAC  
ACAGCACAGAGGGCAGCATGGAAGAGCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC  
ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC  
AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG  
GTGTCAGAGAAGCACCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAAGTCA  
GCACAGAATGCTGGCTCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA  
CAGCAGTCATCCCACCTAAGGAGAAGAAACCTCAGGCCACCCACCCCTGCCCTTTCCAG  
AGCCCCACGACGCAGAGAAACCAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG  
GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG  
TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTC  
TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC  
CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAGGTTCGTGACACGCTTCCCTCCAG  
TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT  
GCCGTGGTGGGCAACGGGGGCATCCTGAACAACCTCCACATGGGCCAGGAGATAGACAGTCA  
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC  
GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT  
CGGGGTTTCAAGAACGTGCCTCTTGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCAC  
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT  
TCTGGTTTCAGGCACAGACCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG  
TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA  
TGGTGGCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTC  
AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT  
CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA  
GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC  
CCGGAACCTGCCAAAGCCAAGAACTGACCCGGGGCCAGGGCTGCCATGGTCTCCTTGCCCTGCTC  
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA  
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT  
GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCTGAGGCCAGG  
GATTTTTTAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCTGCTGAAAAACACTCTT  
CCAGTCCAAAAGCTTCTTGATACAGAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG  
GTTTGAATTCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACCTTCACTAC  
AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG  
TCTTTAAGCTATTTGACAACCTACGTGTTGTAGAAAACCTGATAATAATACAAATGATTGT  
GTCCATGGAAAGGCCAAATAAATTTTCTACAGTGAAAAA

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**FIGURE 242**

MRSC LWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP  
KSQAPTRARRTTIYAE PAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW  
KSPEKEKTMVNTLS PRGQDAGMASGRTEA QSWKSQDTKTTQGN GGQTRKLTASRTVSEKHQG  
KAATTAKTLIPKSQHRMLAPTGA VSTRTRQKGVTTAVIPPEKKPQATPPPAPFQSPTTQRN  
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHF  
NQSEWDRLEHFAPPF GFMELNYSLVQKVVTFRPPVPQQQLLLASLPAGSLRCITCAVVGNGG  
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGF TAFSLTQSLLILGNRGFKNVP  
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL  
RYMKNRFLRSKTL DGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYDTSW  
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRP GPGTAKAKN

**Cytoplasmic Domain:**

amino acids 1-10

**Type II Transmembrane Domain:**

amino acids 11-35

**Lumenal catalytic Domain:**

amino acids 36-600

**Ribonucleotide Reductase small subunit Signature:**

amino acids 481-496

**N-glycosylation Sites:**

amino acids 300-303, 311-314, 331-334, 375-378, 460-463

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**FIGURE 243**

CGATGCGCGGACCCGGGCACCCCCTCCTCCTGGGGCTGCTGCTGGTGCTGGGGCCTTCGCCG  
GAGCAGCGAGTGGAATTGTTCCCTCGAGATCTGAGGATGAAGGACAAGTTTCTAAACACCT  
TACAGGCCCTCTTTATTTTAGTCCAAAGTGCAGCAAACACTTCCATAGACTTTATCACAACA  
CCAGAGACTGCACCATTCTGCATACTATAAAAGATGCGCCAGGCTTCTTACCCGGCTGGCT  
GTCAGTCCAGTGTGCATGGAGGATAAGTGAGAGACCGTACAGGAGCAGCACACCAGGAGCC  
ATGAGAAGTGCCTTGGAACCAACAGGGAAACAGAACTATCTTTATACACATCCCCTCATGG  
ACAAGAGATTTATTTTTGCAGACAGACTCTTCATAAGTCCTTTGAGTTTTGTATGTTGTTG  
ACAGTTTGCAGATATATATTCGATAAATCAGTGTACTTGACAGTGTTATCTGTCACTTATTT

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**FIGURE 244**

MRGPGHPLLLGLLLVLGSPQEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFRLYHNT  
RDCTIPAYYKRCARLLTRLAVSPVCMDK

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**FIGURE 245**

GGGCTGGGCCCCGCCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG  
CCCCACCCCGGCCGCGCCCAGCCCCACCATGCCACCCGCGGGGCTCCGCCGGGCCGCGCCG  
CTCACCGCAATCGCTCTGTTGGTGCTGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT  
GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT  
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG  
CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT  
CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTCTGTTCCCTGTTGCTACCTGT  
ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC  
CCAGTGCAGCCAGTATACCCATACCCCCAGGACCCCCAAAGCTGGCCCTGCACCCCCACAGCC  
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC  
CAGTCTACAACCCTGCAGCTCCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC  
TGAGGAACCAGCCATGTCTCTGCTGCCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT  
CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA  
GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA  
ACTATGAGGGGTGGGGGGAGGGCTTGGAATTATGGGCTATTTTACTGGGGGCAAGGGAGG  
GAGATGACAGCCTGGGTACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG  
CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGGTGGGGGGAGGGAGGAGGT  
TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG  
CTAGATTAAAGCTGTAAAGACAAA

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**FIGURE 246**

MPPAGLRRAAPLTAIALLLVLGAPLVLAGEDCLWYLDNRNGSWHPGFNCEFFTFCCGTCYHRYC  
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLLSCCYLYRRRQQLQSP  
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPP  
YMPPQPSYPGA

**Transmembrane Domains:**

amino acids 10-28, 85-110

**N-glycosylation Site:**

amino acids 38-41

**N-myristoylation Sites:**

amino acids 5-10, 88-93

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**FIGURE 247**

GGGGGAGCTAGGCCGGCGGCAGTGGTGGTGGCGGGCGGCGCAAGGGTGAGGGCGGCCCCAGAA  
CCCCAGGTAGGTAGAGCAAGAAGATGGTGTCTTCTGCCCCCTCAAATGGTCCCTTGCAACCATG  
TCATTTCTACTTTCCTCACTGTTGGCTCTCTTAAGTGTGTCCACTCCTTCATGGTGTGACAG  
CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCTTGGAATAAAATACGACTTC  
CTGAGTACGTACATCCAGTTCATTATGATCTCTTGATCCATGCAAACCTTACCACGCTGACC  
TTCTGGGGAACACGAAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCCTGCA  
TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG  
AAGAACCCTGCAGGTCTGGAACACCCCCCTCAGGAGCAAAATGCACTGCTGGCTCCCGAG  
CCCCCTCTTGTCGGGGCTCCCGTACACAGTTGTCACTTCACTATGCTGGCAATCTTTCGGAGAC  
TTTCCACGGATTTTACAAAAGCACCTACAGAACCAAGGAAGGGGAAGTGAAGGATACTAGCAT  
CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCTGCTTTGATGAACCTGCCTTC  
AAAGCAAGTTTCTCAATCAAAATTAGAAGAGAGCCAAGGCACCTAGCCATCTCCAATATGCC  
ATTGGTGAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTGATGTCACTGTGA  
AGATGAGCACCTATCTGGTGGCCTTCATCATTTCAGATTTTGAGTCTGTGAGCAAGATAACC  
AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC  
ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTTCAGCATACCGTATCCCC  
TACCCAAACAAGATCTTGCTGCTATTCCCGACTTTTCACTGCTGGTGTATGGAAAATCGGGGA  
CTGACAACATATAGAGAATCTGCTCTGTTGTTGATGCAGAAAAGTCTTCTGCATCAAGTAA  
GCTTGGCATCACAGTGACTGTGGCCCATGAACCTGGCCACCAGTGGTTTGGGAACCTGGTCA  
CTATGGAATGGTGGAAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG  
TCTGTCACTGTGACCCATCCTGAAGTGAAGTTGGAGATTATTTCTTTGGCAAATGTTTGA  
CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCTGTGTCTACACCTGTGGAAAATCCTG  
CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGTATTCTGAATATG  
CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAGTGGTATTGTACAGTATCTCCAGAAGCA  
TAGCTATAAAAATACAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG  
ATGGTGTAAAAGGGATGGATGGCTTTTGCTCTAGAAGTCAACATTCATCTTCATCCTCACAT  
TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGTTT  
TCCCCTAATAACCATCACAGTGAGGGGGAGGAATGTACACATGAAGCAAGAGCACTACATGA  
AGGGCTCTGACGGCGCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTCATCACC  
AGCAATCCAACATGGTCCATCGATTTTGTCTAAAACAAAAACAGATGTGCTCATCCTCCC  
AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG  
AGGATGATGGATGGGACTCTTGTACTGGCCTTTTAAAGGAACACACACAGCAGTCAAGCAT  
AATGATCGGGCAAGTCTCATTAACAATGCAATTCAGCTCGTCAGCATTGGGAAGCTGTCCAT  
TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAACTGAAATTATGCCCGTGTTC  
AAGGTTTGAATGAGCTGATTCCTATGTATAAGTTAATGGAGAAAAGAGATATGAATGAAGTG  
GAACTCAATTCAAGGCCTTCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG  
GACAGACGAGGGCTCAGTCTCAGAGCAAAATGCTGCGGAGTGAACACTACTCCTCGCCTGTG  
TGCACAACATATCAGCCGTGCGTACAGAGGGCAGAAGGCTATTTTCAGAAAGTGAAGGAATCC  
AATGGAACCTTGAGCCTGCCTGTGACGTGACCTTGGCAGTGTGTTGCTGTGGGGGCCAGAG  
CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTTCTTTGTCCAGTACTGAGAAAA  
GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT  
GAAAGCTTTAAGGGAGATAAAAATAAAACTCAGGAGTTTCCACAAATCTTACACTCATTGG  
CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAACTGGAACAACTTG  
TACAAAAGTTTGAACCTGGCTCATCTTCCATAGCCACATGGTAATGGGTACAACAAATCAA  
TTCTCCACAAGAACACGGCTTGAAGAGGTAAAAGGATTCTTCAGCTCTTTGAAAGAAAATGG  
TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATGAAAGAAAACATCGGTTGGATGG  
ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAGGCTTGAACGTATGTAAAAA  
TTCCCTCCCTTGCCCGGTTCTGTTATCTCTAATCACCACATTTTGTGAGTGTATTTTCAA  
ACTAGAGATGGCTGTTTTGGCTCCAACCTGGAGATACTTTTTTCCCTTCAACTCATTTTTTGA  
CTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTCATGAATGGGCTTTTTTCATGAATGGGCTA  
TCGCTACCATGTGTTTTGTTTCATCACAGGTGTTGCCCTGCAACGTAAACCCAAGTGTGGGT  
TCCCTGCCACAGAAGAATAAAGTACCTTATTCTTCTCAAAAAAAAAAAAAAAAAAAAAA



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**FIGURE 248**

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH  
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE  
HPPQEQIALLAPEPLLVLGYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA  
ARMAFPFCDEPAFKASF SIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA  
FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLEFYEDYFSIPYPLPKQDLAA  
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL  
WLNEGFAKFMEFVSVSVTHPELKVG DYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD  
DVS YDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG  
FCSRSQHSSSSSHWHQEGVDVKTMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD  
TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL  
TGLLKGTHTAVSSNDRASLINNAFQLV SIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP  
MYKLMEKRD MN EVETQFKAFLIRLLRDLIDKQTTWTDEGSVSEQMLRSELLLLACVHNYQPCV  
QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALC  
RTQNKEKLQWLLDESFKGDKIKTQEFQIILTIGRNPVGYPLAWQFLRKNWNKLVQKFELGS  
SSIAHVMGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQTIETIEENIGWMDKNFDKIR  
VWLQSEKLERM

**Signal peptide:**

amino acids 1-34

**N-glycosylation sites:**

amino acids 70-74, 154-158, 414-418, 760-764, 901-905

**Neutral zinc metallopeptidases, zinc-binding region signature:**

amino acids 350-360

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**FIGURE 249**

CAGCCACAGACGGGTCATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCAC  
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC  
GACCTACCCCGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA  
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG  
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC  
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCGCT  
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCCAGTCTGCTTGTCTATGG  
AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT  
GGCCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC  
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCCGTGGGTATGACTGAGA  
ACTGCAATAGGAAAGATTTTCTGACCTGTCATCGGGGACCACCATTATGACACACGGAAAC  
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT  
GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG  
GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCTCCTGGG  
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG  
CAGCGTTCTGCTGAACTCCCTCCCTCCTCAAGCTGCCCCTGTCCCAGGAGACCGGCAGTGTC  
CTACCTGTGTGCAGCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG  
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAAT  
GAGCATTCAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTTGAACCACACCAGACAAATCG  
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT  
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG  
GTGGGGAGTGGTTTGCCCTTCCTGCTTAACTCTATTACCCCCACGATTCTTCACCGCTGCTGA  
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTTC  
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTCATATCTACTCACCTAACAGCA  
ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG  
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

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**FIGURE 250**

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLI  
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP  
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRRLRGGGIFSNLRVQGCMPQPGCN  
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSENTEMCEVGQVCQETL  
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLNCSASSSSVLLN  
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGC  
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLES LTWGVGLALAPALWWGVVC  
PSC

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**FIGURE 251**

GCACGGGACAGGACGCCCCGTTTCGCCTAGCGCGTGCTCAGGAGTTGGTGTCTGCCTGCGCT  
CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG  
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG  
CCTCAAAGGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCCGGACGGCCTGGAAGAGTCG  
GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTTCGTCTAT  
GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC  
TGGTCTTAATGGAGAACCAGGCCTCCCATGTGAGTGCAGCCAGCTGCGCAAGGCCATCGGGG  
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTGCGC  
GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA  
CGCCCAGCTGTCTTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA  
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCGTGTCTTCATCGGCATCAAC  
GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA  
GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGAGATGGTGGCCT  
CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG  
GAGAACATGTGAGCCTCAGGCTGGGGCTGCCATTGGGGGCCCCACATGTCCCTGCAGGGTT  
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG  
GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG  
AAAGTGTTCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA  
ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC  
TATACAATAAAATCTTTAAGTAGTGCAGTAGTTAAGTCCAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 252**

MRGNLALVGVLISLAFLLPSGHPQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG  
PTGEKGMGDKGQKGSVGRHGKIGPIGSKGEKGDSDIGPPGPNGEPGLPCECSQLRKAIGE  
MDNQVSQLTSELKFINKAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAAN  
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVEMVAS  
GGWNDVACHTTMYFMCEFDKENM

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**FIGURE 253**

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG  
CACCAGTGTGTGAGGGGAGCAGGCAGCGTCTAGCCAGTTCCTTGATCCTGCCAGACCACC  
CAGCCCCCGGCACAGAGCTGCTCCACAGGCACCATGAGGATCATGCTGCTATTCACAGCCAT  
CCTGGCCTTCAGCCTAGCTCAGAGCTTTGGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG  
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC  
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA  
GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA  
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCCTCGGCCC  
CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC  
TTTATTAAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT  
ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC  
TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTCTCTTCCCTGTTCTTGT  
AACATTCTTGTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA  
TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT  
CCTACATTAAAAATATAATGTCTCTCTCTATTCCCTCAACAATAAAGGATTTTTGCATATGAA  
AAA

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**FIGURE 254**

MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK  
ALSQASTDPKESTSPEKRDMDHDFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK  
SSLGTEEQRPL

**Important features:****Signal peptide:**

amino acids 1-18

**Tyrosine kinase phosphorylation site.**

amino acids 36-45

**N-myristoylation site.**

amino acids 33-39, 59-65

**Amidation site.**

amino acids 90-94

**Leucine zipper pattern.**

amino acids 43-65

**Tachykinin family signature.**

amino acids 86-92

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**FIGURE 255**

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCCTGTGCCTGCTGTGCC  
CGCGCTGTGCGCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG  
GAGCCCTGCGGAGAGCTCAAGCGCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC  
CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCGTCCTGGGTGGTGTATCCCCTTGGGGC  
TGCTGTTCTGCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG  
CTGCTCAGCAAATACCAGCACAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA  
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT  
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC  
CTGGGCCACCAGCCTGCTCTGTTCCCCAGCCAGCTCTGTTCCCCAGCCAGTGCGTGTGATGG  
CTGGCTCAGGGTCTCCTCTGGCAGGGGAGGATCCCGGCTCTGTTCTGTTTTGTTTGTGTTGTT  
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG  
AAACCTTAGACTCCCGGGGTAAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACACAG  
GCATGCACCATGGTGCCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT  
TGCCCAGGCTGGTCTTGAACCTCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG  
CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA  
ACAACACACGTGGGTTCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC  
TCCACTGGGAACACAGCTCTCAGCCTTTCCACCTGGAGGCAGAGTGGGGAGGGGGCCAGGG  
CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC  
CTTAGCCCGTGTGAGCCTCACTTTCCACTTGGAGAGTCCTTCCTCGCGTGGTTGCCATGACT  
GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCTTAGG  
CTTTGCTAACCGGGAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT  
GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG  
TGGAAACTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG  
GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTCAGCTATGAATGGCTT  
TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAATC  
CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG  
GTGGAGGTGGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC  
AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAA



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**FIGURE 256**

MSCVLGGVIFLGLLFLVCGSQGYLLPNVTLLLEELLSKYQHNEHSRVRRRAIPREDKEEILML  
HNKLRGQVQPQASNMEYMVSAAGSGRRGWHRGWGLGHQPALFPSQLCSPASACDGWLRVSSGR  
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

**Important features:**

**Signal peptide:**

amino acids 1-22

**N-glycosylation site.**

amino acids 27-31, 41-45

**N-myristoylation site.**

amino acids 126-132, 140-146

**Amidation site.**

amino acids 85-89

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**FIGURE 257**

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGG  
GTCTGGGCTGCCCCTTGTCCTCCTCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGG  
GTATGACTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGC  
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTTCAGGGACCAGCGTCAC  
CCTCCACCATGCAAGATCTCAACACCATGTTGTCTGCAACACATTGACAGCCATTGAAGCCTG  
TGTCTTCTTGGCCCGGGCTTTTGGGCCGGGGATGCAGGAGGCAGGCCCCGACCCTGTCTTT  
CAGCAGGCCCCCACCCTCCTGAGTGGCAATAAATAAAATTCGGTATGCTG

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**FIGURE 258**

MSGGLPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSYESSFLELLEKLCLLLHLPST  
VTLHHARSQHHVVCNT

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**FIGURE 259**

AATTGTATCTGTGTAATGTTAAAACAAACGAAATAAAATAGAAGGAAAACTTTCTGAGTTT  
CAAAAACAACAGACTAGTACTCTAAAGAACTCTTTAAAACAATTAAGTGTAGGATTGCAGT  
TATGATTGGATATTATTTAATTCTGTTTCTGATGTGGGGTTCCTCCACTGTGTTCTGTGTGC  
TATTAATATTTACCATTGCAGAAGCTTCATTCAGTGTTGAAAATGAATGCTTAGTGGATCTG  
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTTCCTAATCAATGCAGAGTTCCCCCTCCC  
CTCCGATTGTTCTAAATTAATTGAAAGATGTCTGCTGTGGAAAAGGCATGTATTTAAATCTG  
TATGATTCTCAACCATCTTTAGTTGGGAAAGGTCCTTGAAAGCCAATGGAAATACTTTTTTT  
TTTTCTTGGCACTAATCAAGTGAGTGTTACCTTTTCACTTAGTAGGATGTGTTGTTACGCTA  
GTAAAATAGAAACCTGTGTTTATTCTCAGGTATTTTAGAAACAACAGCCATCATTTTATTTT  
ATGTGTGTGTTCTTGGCTGTATTCATAAATTATATATTTTGGGCTATCAAATATTACTTCAT  
TCAATATAAATAACAATAGTAGAAGTTGTTTACTTAGATATGCTTCTAGTTGCATTTTCTC  
AGCCTATGTAAGACTACTTTGTTGTAATAGCCTTTGAAATTTACAGTACTGTCTCTCTACTA  
TCTTCAGATTACTTGATTCAAATAAACCAATTATGTTTGTAAATTGATATTAATAAAACCAGA  
ATAAAAGTTCATATCTACCC

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**FIGURE 260**

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP  
SDCSK

**Important features:**

**Signal peptide:**

amino acids 1-29

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**FIGURE 261**

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGCCCTTGAGACATCCTT  
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTTTTGCAGGATGATGGTGGCCCTT  
CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCCTTGACAGCTTTTCTGCCCCCGCCGAGTGAC  
CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG  
AAAAATGTACCCAAGCAACGAGGGCATAACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA  
TCTGTCATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGACAGTGGGTAACTT  
GGCACTGAGAGTTGAACGTGCCCAACGGGAGATTGACTACATAACAATACCTTCGAGAGGCTG  
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA  
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC  
TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA  
ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTTGGGAATTTGCAAAC  
ATACGGGCATTTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC  
CTGGCAGGGAACAGGCCAAGTGATCTACAAAGTTTTCTATTTTTTTCATAACCAAGCAACTT  
CTAATGAGATAATCAAATATAACCTGCAGAAGAGGACTGTGGAAGATCGAATGCTGCTCCCA  
GGAGGGGTAGGCCGAGCATTGGTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT  
GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA  
CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTTCATGGGATACCCCATGCAGAAGCCAG  
GATGCTGAAGCCTCATTCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA  
GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC  
CCAATTGTTCTTCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCAGAGAT  
AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAA  
GCTGCCTCTGAAGTAAATGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTT  
TACAGGACAGTGAGGCTATAGCCCCTTCACAATATAGTATCCCTCTAATCACACACAGGAAG  
AGTGTGTAGAAGTGGAATACGTATGCCTCCTTTCCCAAATGTCAGTGCCTTAGGTATCTTC  
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAA  
CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTCTTACT  
GCTCCCCAGCATTTACTGTAACCTCTGCCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGC  
CCCTAATATTACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT  
CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCACTAAAATACTATTAATATTTCTTT  
CTTTTCTTTTCTTTTTTTTTGAGACAAGGTCTCACTATGTTGCCAGGCTGGTCTCAAACCTCC  
AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC  
CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACTCTATTTCCCTAGCCCTGTC  
CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT  
CCAGGTGTGGAGTGTTTGCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG  
TCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC  
TAGAAAATACTACAAATCCCATAGTTTTTTCATTGCCCAAGGAAGCATCAAATACGTATGTT  
TGTTACCTACTCTTATAGTCAATGCGTTCATCGTTTCAGCCTAAAATAATAGTCTGTCCC  
TTTAGCCAGTTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC  
AGAAAACAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTTGTCTTGTCTGCTCTCTGT  
TTCTCTCTTTCTGCTTTAAATTCAATAAAAGTGACACTGAGCAAAAAAAAAAAAAA

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**FIGURE 262**

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQE  
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL  
QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNPKVYLLIGSRNNTV  
WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED  
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKEPGLGVEHSWDT  
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH  
YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK





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**FIGURE 264**

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK  
QYQIRIRKEKPQQHNFTHRLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ  
REHRSMRANVELDHATLVRFSPPDCRAFIWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK  
HKAPVIDIGIANTGKFIMTASSDTPVLIWLSLKGQVLSTINTNQMNNTAAVSPCGRFVASC  
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV  
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH  
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ  
AQETLKS LGALKK

**Important features:****Signal peptide:**

amino acids 1-25

**N-glycosylation site.**

amino acids 76-80, 92-96, 231-235, 289-293, 378-382, 421-425

**Beta-transducin family Trp-Asp repeat protein.**

amino acids 30-47, 105-118, 107-119, 203-216, 205-217, 296-308

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**FIGURE 265**

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG  
CAGTGTTTTGCCTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCC  
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT  
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT  
GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA  
AGCACACACCTGTCCTTGCTTGCCCAACCTGCTGTGCTCCAGGTTCCTGGACGGCAGGTAC  
CGCTGCTCCATGGACTTGAAGAACATCAATTTTTTAGGCGCTTGCCTGGTCTCAGGATACCCA  
CCATCCTTTTCCTGAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGAC  
TCTCCCAGTCCCTACACTGACTACCCTGATCTCTCTTGTCTAGTACGCACATATGCACACAG  
GCAGACATACCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGG  
CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTTCCCTGCTCAGGCTGCCAGAGAGGTGGTA  
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTCTTTCTGGGCCCTG  
CCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTTGGGCACAGGCTCTTGGGT  
GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG  
ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGAC  
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA  
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA  
CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT  
TAACCACTGAAGCCCCCAATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAA  
TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACCTTTCCA  
AGGATCAGCCCTGAGAGCAGGTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG  
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTACAGACCAGGGAGG  
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAA

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**FIGURE 266**

MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHP  
GSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

**Signal peptide:**

amino acids 1-19

**Tyrosine kinase phosphorylation site:**

amino acids 88-95

**N-myristoylation sites:**

amino acids 33-39, 35-41, 46-52

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**FIGURE 267**

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCTTTC  
CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC  
TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG  
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA  
GCAAAGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT  
CCTCTGTCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG  
TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT  
TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAAGTTCTATGGTCCACAAAGGCGGAAGAT  
GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACCTTCTTCCGAGCCTGGAACGGAG  
GCTTCTCTGGAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA  
GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT  
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAATGAT  
TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTACCTGTGTTTCATGGGATGTATT  
GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA  
TTAATGTATTTTAATATTCTGTTTAGGCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGA  
CAAAAATCTGAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA  
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG  
TGAGCAAGTCACTTGAGGTGCGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTC  
TCTACTAAAAATACAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG  
GGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA  
CACCCTGTATTCCAGCCTGGGTGACTGAGACTCTAACTAA

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**FIGURE 268**

MSFLQDPSFFTGMWSIGAGALGAAALALLANTDVFLSKPQKALEYLEDIDLKTLEKEPR  
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF  
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEFILGGVFV  
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

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**FIGURE 269**

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCCG  
GGCCAGGTGCCCCGTGCGAGGTGCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA  
AGCCCCCTTCCTCGGCGCTGCCAACCCGCCACCCAGCCCATGGCGAACCCCGGGCTGGGGCTG  
CTTCTGGCGCTGGGCCTGCCGTTCTGCTGGCCCGCTGGGGCCGAGCCTGGGGGCAAATACA  
GACCACTTCTGCAAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATG  
GCAACCTGCGTCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTTGGCTGCCTTG  
CTCCTGGCTGTGGGGCTGGCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGG  
CACCTACCGGCCCAGTAGCGAGGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCTCAGG  
ACTCCAAGGAGACGGTGCAGGGCTGCCTGCCATCTAGGTCCCCTCTCCTGCATCTGTCTCC  
CTTCATTGCTGTGTGACCTTGGGGAAAGGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAG  
TGCTTAATAGCAGGGAAGAAGTACTTCAAAGACTCTGCCCTGAGGTCAAGAGAGGATGGG  
GCTATTCACCTTTTATATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAAAA

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**FIGURE 270**

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSSSTSSSSDGNLRPEAITAIIV  
VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

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**FIGURE 271**

AATATATCATCTATTTATCATTAATCAATAATGTATTCTTTTATTCCAATAACATTTGGGTT  
TTGGGATTTTAATTTTCAAACACAGCAGAAATGACATTTTTTCTGTCACTATTATTATTGTTG  
GTATGTGAAGCTATTTGGAGATCCAATTCAGGAAGCAACACATTGGAGAATGGCTACTTTCT  
ATCAAGAAATAAAGAGAACCACAGTCAACCCACACAATCATCTTTAGAAGACAGTGTGACTC  
CTACCAAAGCTGTCAAACCACAGGCAAGGGCATAGTTAAAGGACGGAATCTTGACTCAAGA  
GGGTTAATTCTTGCTGAAGCCTGGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG  
ATTGTAAATTTAAGGCAAATACACATATTAGTATTACCTTAGTGTAATGTATCCCTGTCATA  
TATACAATAAGGTGAAATTATAAGTACCCTATGCAGTTGGCTGGACAGTTCTAAATTGGACT  
TTATTAATTTTTTAAATCAGTAACTGATTTATCACTGGCTATGTGCTTAGATCTACAGGAGA  
TCATATAATTTGATACAAATAAAAGAAAAGTGTTCTCTCCCCTTACAGAATTGACATTTTAA  
ATGCGATACAGTTAGAATAGGAAATATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA  
AGAAGGGAAAATGTTGCCAAGGAAAAA



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**FIGURE 272**

MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK  
GIVKGRNLDSRGLILGAEAWGRGVKKNT

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**FIGURE 273**

GCCAGGAATAACTAGAGAGGAACA**AT**GGGGTTATTTCAGAGGTTTTGTTTTCTCTTAGTTCT  
GTGCCTGCTGCACCAAGTCAAATACTTCTTCATTAAAGCTGAATAATAATGGCTTTGAAGATA  
TTGTCAATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAATAATTGAACAAATAGAGGAT  
ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAGATTTTTTTTCAAAAA  
TGTATCTATATTAATTCCTGAGAATTGGAAGGAAAAATCCTCAGTACAAAAGGCCAAAACATG  
AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCCAGGTAGAGATGAACCA  
TACACCAAGCAGTTCACAGAATGTGGAGAGAAAGGCGAATACATTCACCTTCACCCCTGACCT  
TCTACTTGGAAAAAACAATAATGAATATGGACCACAGGCAAACTGTTTGTCCATGAGTGGG  
CTCACCTCCGGTGGGGAGTGTGATGAGTACAATGAAGATCAGCCTTTCTACCGTGCTAAG  
TCAAAAAAATCGAAGCAACAAGGTGTTCCGCAGGTATCTCTGGTAGAAATAGAGTTTATAA  
GTGTCAAGGAGGCAGCTGTCTTAGTAGAGCATGCAGAATTGATTCTACAACAAAACCTGTATG  
GAAAAGATTGTCAATTCCTTCTGATAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG  
CAAAGTATTGATTCTGTTGTTGAATTTTGTAAACGAAAAAACCATAATCAAGAAGCTCCAAG  
CCTACAAAACATAAAGTGCAATTTTAGAAGTACATGGGAGGTGATTAGCAATTCCTGAGGATT  
TTAAAAACACCATACCCATGGTGACACCACCTCCTCCACCTGTCTTCTCATTGCTGAAGATC  
AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT  
AAATCGAATGAATCAAGCAGCAAAACATTTCTGCTGCAGACTGTTGAAAATGGATCCTGGG  
TGGGGATGGTTCACCTTTGATAGTACTGCCACTATTGTAATAAGCTAATCCAAATAAAAAGC  
AGTGATGAAAGAAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACCTCCAT  
CTGCTCTGGAATTAAATATGCATTTTCAGGTGATTGGAGAGCTACATTCCCAACTCGATGGAT  
CCGAAGTACTGCTGCTGACTGATGGGGAGGATAACACTGCAAGTCTTGATTTGATGAAGTG  
AAACAAAGTGGGGCCATTGTTTATTTATGCTTTGGGAAGAGCTGCTGATGAAGCAGTAAT  
AGAGATGAGCAAGATAACAGGAGGAAGTCATTTTATGTTTTCAGATGAAGCTCAGAACAATG  
GCCTCATTGATGCTTTTGGGGCTCTTACATCAGGAAATACTGATCTCTCCAGAAAGTCCCTT  
CAGCTCGAAAGTAAGGGATTAACTGAATAGTAATGCCTGGATGAACGACACTGTCATAAT  
TGATAGTACAGTGGGAAAGGACACGTTCTTTCTCATCACATGGAACAGTCTGCCTCCAGTA  
TTTCTCTCTGGGATCCCAGTGGAACAATAATGGAAAAATTTACAGTGGATGCAACTTCCAAA  
ATGGCCTATCTCAGTATTTCCAGGAACCTGCAAGGTGGGCACCTGGGCATACAATCTTCAAGC  
CAAAGCGAACCCAGAAACATTAACATTTACAGTAACCTCTCGAGCAGCAAAATCTTCTGTGC  
CTCCAATCACAGTGAATGCTAAAATGAATAAGGACGTAAACAGTTTCCCCAGCCCAATGATT  
GTTTACGCAGAAATCTACAAGGATATGTACCTGTTCTTGGAGCCAATGTGACTGCTTTTCA  
TGAATACAGAATGGACATACAGAAGTTTGGAACTTTGGATAATGGTGCAGGCGCTGATT  
CTTTCAAGAATGATGGAGTCTACTCCAGGTATTTTACAGCATATACAGAAAAATGGCAGATAT  
AGCTTAAAAGTTTCGGGCTCATGGAGGAGCAAACACTGCCAGGCTAAAATTACGGCCTCCACT  
GAATAGAGCCGCGTACATACCAGGCTGGGTAGTGAACGGGGAAATTGAAGCAAACCCGCCAA  
GACCTGAAATTGATGAGGATACTCAGACCACCTTGGAGGATTTAGCCGAACAGCATCCGGA  
GGTGCATTTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCCTGACCAATACCCACCAAGTCA  
AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTCTTACATGGACAGCACCAG  
GAGATAATTTTGTATGTTGAAAAAGTTCAACGTTTATATCATAAGAATAAGTGCAAGTATTCTT  
GATCTAAGAGACAGTTTTGTATGATGCTCTTCAAGTAAATACTACTGATCTGTACCCAAAGGA  
GGCCAACTCCAAGGAAAGCTTTGCATTTAAACCAGAAAAATATCTCAGAGAAAAATGCAACCC  
ACATATTTATTGCCATTAAAAGTATAGATAAAAGCAATTTGACATCAAAAGTATCCAACATT  
GCACAAGTAACCTTTGTTTATCCCTCAAGCAAATCCTGATGACATTGATCCTACACCTACTCC  
TACTCCTACTCCTACTCCTGATAAAAGTCATAATTCTGGAGTTAATATTTCTACGCTGGTAT  
TGTCTGTGATTGGGTCTGTTGTAATTGTTAACTTTATTTTAAAGTACCACCATTT**GA**ACCTTA  
ACGAAGAAAAAATCTTCAAGTAGACCTAGAAGAGAGTTTTAAAAAACAACAAATGTAAGT  
AAAGGATATTTCTGAATCTTAAATTCATCCCATGTGTGATCATAAACTCATAAAAATAATT  
TTAAGATGTCGGAAAAGGATACTTTGATTAAATAAAAAACACTCATGGATATGTAAAACTGT  
CAAGATTAAAATTTAATAGTTTTCATTTATTTGTTATTTTATTTGTAAGAAATAGTGATGAAC  
AAAGATCCTTTTTTCATACTGATACCTGGTTGTATATTATTTGATGCAACAGTTTTCTGAAAT  
GATATTTCAAATTGCATCAAGAAATTAATCATCTATCTGAGTAGTCAAAATACAAGTAA  
GGAGAGCAATAAACAAACATTTGGAAAAAATAAAAAAAAAAAAAAAAAAAAAA  
AAA

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**FIGURE 274**

MGLFRGFVFLVLCLLHQSNSTFIKLNNGFEDIVIVIDPSVPEDEKIIIEQIEDMVTTASTY  
LFEATEKRFFFFKNVSILIPENWKENPQYKRPKHENHKKHADVIVAPPTLPGRDEPYTKQFTEC  
GEKGEYIHFTPDLLLGGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR  
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDQVQTEKASIMFMQSIDSVE  
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV  
LDKSGSMGGKDRLNRMNQAAKHFLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM  
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTGDGNTASSCIDEVKQSGAIVH  
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQSLQLESKGLT  
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG  
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPI TVNAKMNKDVNSFPSPMIVYAEILQG  
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNQDVYSRYFTAYTENGRYSLKVRAHG  
GANTARLKL RPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRTASGGAFVVSQV  
PSLPLPDQYPPSQITDL DATVHEDKIIILTWTAPGDNFDVGKVQRYIIRISASILDLRDSFDD  
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSNIAQVTLFIP  
QANPDDIDPTPTPTPTPTPDKSHNSGVNISTLVLSVIGSVVIVNFILSTTI

**Signal peptide:**

amino acids 1-21

**Putative transmembrane domains:**

amino acids 284-300, 617-633

**Leucine zipper pattern.**

amino acids 469-491, 476-498

**N-glycosylation site.**amino acids 20-24, 75-79, 340-344, 504-508, 542-546, 588-592,  
628-632, 811-815, 832-836, 837-841, 852-856, 896-900

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**FIGURE 275**

CTCCTTAGGTTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAAGACCATACGTCCTCCCG  
GGCAGGGGGTGACAACAGGTGTCATCTTTTGTATCTCGTGTGTGGCTGCCTTCTTATTTCAAGGAAAG  
ACGCCAAGGTAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACC  
CCCAGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACTT  
GTGGTTGGAGGAGAGAACCCTTTGTGGGGCTGCGTTCTCTTAGCAGTGCTCAGAACTGACTTGCCTGA  
GGGTGGACCAGAAAGGAAAGGTCCCTCTTGTCTGTGGCTGCACATCAGGAAGGCTGTGATGGG  
AATGAAGGTGAAAACCTTGGAGATTTCACTTCAGTCATTGCTTCTGCCTGCAAGATCATCTTTAAAA  
GTAGAGAAGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACTCGTTCTAGAAGGAAATGGATG  
CAAGCAGCTCCGGGGGGCCCCAAACGCATGCTTCTGTGGTCTAGCCCAGGGAAGCCCTTCCGTGGGG  
GCCCCGGCTTTGAGGGATGCCACCGCTTCTGACGTCATGGCTGATTCTGAATGATGATGGTTCCGC  
GGGGCTGTCTGCGTGGATTTCCCGGGTGGTGGTTTTGCTGGTGTCTCTCTGTGTGCTATCTCTGT  
CCTGTACATGTTGGCCTGCACCCCAAAGGTGACGAGGAGCAGCTGGCACTGCCAGGGCCAACAGC  
CCCACGGGGAAGGAGGGGTACCAGGCCGTCTTTCAGGAGTGGGAGGAGCAGCACCGCAACTACGTGA  
GCAGCCTGAAGCGGCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGCAGGAGAGGAA  
TGGGCAGTACCAAGCCAGCGATGCTGCTGGCCTGGGTCTGGACAGGAGCCCCCAGAGAAAACCCAG  
GCCGACCTCCTGGCCTTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGG  
CCACAGAGTATGCAGCAGTGCCTTTTCGATAGCTTACTCTACAGAAGGTGTACCAGCTGGAGACTGG  
CCTTACCCGCCACCCCGAGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGGAGGCCATT  
GAATCAGCCTTGGAGACCCTGAACAATCTGCAGAGAACAGCCCCAATCACCGTCTTACACGGCCT  
CTGATTTTCATAGAAGGGATCTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAA  
AGGGGACCACAAACACGAATTCAAACGGCTCATCTTATTTTCGACCATTACGCCCCATCATGAAAGTG  
AAAAATGAAAAGCTCAACATGGCCCAACACGCTTATCAATGTTATCGTGCCTTAGCAAAAAGGGTGG  
ACAAGTTCCGGCAGTTCATGCAGAATTTCAAGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCT  
CACTGTTGTTTACTTTGGGAAAGAAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAA  
GCTGCCAACTTCAGGAACCTTACCTTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTG  
ATGTTGGAGCCCGCTTCTGGAAGGGAAGCAACAGTCCCTTCTCTTTTTCTGTGATGTGGACATCTACTT  
CACATCTGAATTCCTCAATACGTGTAGGCTGAATACACAGCCAGGGAAGAAGGTATTTTATCCAGTT  
CTTTTCAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCCTCCCTTGGAAACAGC  
AGCTGGTCATAAAAGAAAGGAAACTGGATTTTGGAGAGACTTTGGATTTGGGATGACGTGTGATATCG  
GTCAGACTTCATCAATATAGGTGGGTTTGATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCAC  
CTTTATCGCAAGTATCTCCACAGCAACCTCATAGTGGTACGGACGCCTGTGCGAGGACTCTTCCACC  
TCTGGCATGAGAAGCGCTGCATGGACGAGCTGACCCCGAGCAGTACAAGATGTGCATGCAGTCCAA  
GGCCATGAACGAGGCATCCACGGCCAGCTGGGCATGCTGGTGTTCAGGCACGAGATAGAGGCTCAC  
CTTCGCAAACAGAAACAGAAGACAAGTAGCAAAAAACATGAACCTCCAGAGAAGGATTGTGGGAGA  
CACTTTTTCTTTCTTTTGCAATTACTGAAAGTGGCTGCAACAGAGAAAAGACTTCCATAAAGGACG  
ACAAAAGAATTGGACTGATGGGTGAGAGATGAGAAAGCCTCCGATTTCTCTCTGTGGGCTTTTTAC  
AACAGAAATCAAAATCTCCGCTTTGGCTGCAAAAGTAACCCAGTTGCACCTGTGAAGTGTCTGACA  
AAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTGTGGAGGTTTTGATGGTGTTTACAATACACT  
GAGACCTGTTGTTTTGTGTGCTCATTGAAATATTCATGATTTAAGAGCAGTTTTGTAAAAAATTCAT  
TAGCATGAAAGGCAAGCATATTTCTCCTCATATGAATGAGCCTATCAGCAGGCTCTAGTTTCTAGG  
AATGCTAAAAATATCAGAAAGGCAAGGAGAGGAGATAGGCTTATTATGATACTAGTGAGTACATTAAGTA  
AAATAAAATGGACCAGAAAAGAAAAGAAACCATAAATATCGTGTGATATTTTCCCAAGATTAACCA  
AAAATAATCTGCTTATCTTTTTGGTTGTCTTTTAACTGTCTCCGTTTTTTTTCTTTTATTTAAAAAT  
GCACACTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTACCCTTTGCAAGCCTTACAAAGAGA  
GCACAAGTTGGCCTACATTTTTTATATTTTTTAAGAAGATACTTTGAGATGCATTATGAGAACTTTCA  
GTTCAAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATGCTGATTCTGTGAGGCACTGAAT  
GTCAGGCATTGAGACATAGGGAAGGAATGGTTTGTACTAATACAGACGTACAGATACTTTCTCTGAA  
GAGTATTTTTCGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATGACACTTTCTGCTTTACAGAA  
AAGGAACTCATTACAGACTGGTGATATCGTGATGTACCTAAAAGTCAGAAACCACATTTTCTCCTCA  
GAAGTAGGGACCGCTTCTTACCTGTTTAAATAAACCAAGTATACCGTGTGAACCAAAACATCTCT  
TTTCAAAACAGGGTGCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAATGGAGAAAATATATATAT  
ATATATATATATTTGTGAAAGATCAATCCATCTGCCAGAAATCTAGTGGGATGGAAGTTTTGCTACAT  
GTTATCCACCCAGGCCAGGTGGAAGTAACCTGAATTATTTTTTAAATTAAGCAGTTCTACTCAATCA  
CCAAGATGCTTCTGAAAATTGCATTTTATTACCATTTCAAACTATTTTTTAAAAATAAATACAGTTA  
ACATAGAGTGGTTTCTTCATTTCATGTGAAAATTATTAGCCAGCACCAGATGCATGAGCTAATTATCT  
CTTTGAGTCTTGTCTCTGTTTGTCTACAGTAACCTCATTGTTTAAAGCTTCAAGAACATTCAAGC  
TGTTGGTGTGTTAAAAAATGCATTGTATTGATTGTACTGGTAGTTTATGAAATTTAATTAAACAC  
AGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAATATGATTTGTGGATATGAA

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**FIGURE 276**

MMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQALPRANSPTGKEGYQAVLQ  
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL  
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPV RKDKRDELVEAIES  
ALETNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP  
MKVKNEKLN MANTLINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVK  
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTR  
LNTQPGKKVFYPVLFSQYNPGIIYGHHDVPPLEQQLVIKKETGFWRDFGFGMTCQYRSDFI  
NIGGFDLDIKGWGGEDVHLYRKYLHSNLIVVRTPVRGLFHLWHEKRCMDELTPEQYKMCMQS  
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

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**FIGURE 277**

GAAAGAATGTTGTGGCTGCTCTTTTTCTGGTGA CTGCCATTCATGCTGAACTCTGTCAACC  
AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT  
ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA  
GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT  
ATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC  
AATCAGCCATAAGAATGAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGACCAAAC  
CTGGAATTTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG  
GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTAT  
CAGGGATCTGGCAACGTAGAAGAAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT  
AAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGG  
GGGCATATTAATGATGCCTTCATTGACAGAGGATGAGAGGCTCACCCCTCTCTGAAGGGCTGT  
TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGA CTGCTGAGCATCCTGAAATA  
CCAAGAGCAGATCATATATTTTGTTCACCATTCTTCTTTTGTAATAAATTTTGAATGTGCT  
TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC  
TCAAAATATTCTAAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG  
TAGTTATTGATTTAAGCATTTTTAGAAATAAGATCAGGCATATGTATATATTTTCACACTTC  
AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT  
TGAAAATGGATCCTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG  
TGAGAAGTAATTATTGTAAATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATT  
TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC  
AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG  
TAATAATCATCTCTTTTTTAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 278**

MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP  
NREATEISHVLLCNVTQRVSFVFTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE  
FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC  
ENMITIENGIPSDPLDMKGGILMMP

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**FIGURE 279**

AACTCAAACCTCCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG  
GTGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTCCATGT  
ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGG  
CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC  
TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCCCTGTGGGTGATGCTCTAACAGTGACCTGGA  
ATTTTCGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC  
CAACCCATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA  
TGCCTCCATCCTTCTCTGGAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA  
AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA  
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT  
AATAGTAATTGTAGTGGTCCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC  
ATAAAGTGGTGGAGATAAAATCAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT  
GTTTATTTAGAAGACACAGACTAACAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA  
GAACCCTAGTATTTCTTGAAGTTAATGGAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT  
TTTCCAACCAAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC  
AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGA  
GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAA  
GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC  
AATTTGTCTGTTACATTTCCCTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA  
ATGTGTTTACTCTCTTTCCCTTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG  
TTTCTGATTAACAGTAAATCCTAAATTCAACTGTTAAATGACATTTTTATTTTTATGTCTC  
TCCTTAACATATGAGACACATCTTGTTTTACTGAATTTCTTTCAATATTCCAGGTGATAGATT  
TTTGTCG



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**FIGURE 280**

MYGKSSTRAVLLLLGIQLTALWPAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT  
WNFRPLDGGPEQFVFYYHIDPFQPMSEGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ  
VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVLFFQHYRKKRWAER  
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

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**FIGURE 281**

GCATTTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACCATGAAGTTCTTAGCAGTCCTGGT  
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG  
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT  
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG  
TAAAGACATTCCAGTTTTACCCAAATGGGTTGGGGATCTCCCGAATGGTAGAGTGTGTCCCTT  
GAGATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACATTCATGCTTCCTGTGATTTT  
ATCCAACACTTACCTTGCCCTACGATATCCCCTTTATCTCTAATCAGTTTATTTTCTTTCAA  
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

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**FIGURE 282**

MKFLAVLVLLGVSI FLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTAT  
TAASTTARKDIPVLPKWVGDL PNGRVCP

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**FIGURE 283**

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC  
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAATGC  
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTACGGTGGCCTGGTCCCTCCTTGCCGAGAGA  
GTGTCCTGGGTCAGGGACGCAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC  
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG  
GACAGTTCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGGCCAGTCCAGGGTGGGGGGCG  
GCAAACCTCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCCAGCTCCT  
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAGTTAAAACCACAGGCTGG  
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA  
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTTACCACATTAGCAATTAAACTGAGAAAT  
GGGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT  
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA  
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG  
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT  
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA

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**FIGURE 284**

MLPPALPPALVFTVAWSLLAERVSQVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG  
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ

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**FIGURE 285**

GTCATGCCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTGACCCGGCCTGCCTCA  
GCGGCCCCCATGGGCGGCCAGAACTGGCACAGCATGAGGAGCTGACCCTGCTCTTCCATGG  
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCACGGAGGGACGGCTGACAA  
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTCAGC  
CGGGGCCGGGATGCAGCCAGGAACTTCGGGCAAGCCTGTTGGGAGACTCAGATGGAGGAGGA  
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCCAGGCACAGA  
AGGTGCTACGGGACAGCGTGCAGCGGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGGCCCT  
GCCTACCGAGAATTTGAGGTCTTAAAGGCTCACGCTGACAAGCAGAGCCACATCCTATGGGC  
CCTCACAGGCCACGTGCAGCGGCAGAGGCGGGAGATGGTGGCACAGCAGCATCGGCTGCGAC  
AGATCCAGGAGAGACTCCACACAGCGGCGCTCCCAGCCTGAATCTGCCTGGATGGAAGTGA  
GACCAATCATGCTGCAAGGAACACTTCCACGCCCCGTGAGGCCCTGTGCAGGGAGGAGCTG  
CCTGTTCACTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGAGCAGAGACAGAC  
GCAGGCGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA  
CCCTTTCATGCCTACACACCCCTCATTAAGCAGAGTCGTGGCATTTCAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 286**

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK  
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK  
VL RDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ  
IQERLHTAALPA

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**FIGURE 287**

GGCAACATGGCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT  
CCTGGTGATCACCTTACTCCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA  
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC  
TGGACAGAAGTCAATGCCTTGAAGGAAATTCAGCCCTGCAGACAGTCTGTCTCCGAGGCAC  
TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG  
AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC  
CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA  
CATGGTCACGGAAGGCAAGTTTGTGACGTCAACGGAATCGCTATCTCCTTCCTCAACTGGG  
ACCGTGCACAGCCTAACGGTGGCAAGCGAGAAAACCTGTGTCTGTTCTCCAATCAGCTCAG  
GGCAAGTGGAGTGATGAGGCCTGTGCGAGCAGCAAGAGATACATATGCGAGTTCACCATCCC  
TAAATTAGGTCTTTCTCCAATGTGTCTCCAAGCAAGATTCATCATAACTTATAGGTTTCATGA  
TCTCTAAGATCAAGTAAAAATCATAATTTTACTTATTAAAAAATTGCAACACAAGATCAAT  
GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT  
TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT  
AAACAGACTAAAATCTTTCTCTCTAGTCTTTCTCACTTGTACAAACCCAGTTTGTTCAAA  
AAATCACAGTAGCAATGCAACTCATCACTCTAGAAAAGCAAGCTTAGGCTACCTGAAAGATT  
TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATTCCCTACATCAGAGACTCTAGGT  
GCTATATAATCCAAAACTTTTCAGCCTGTGCTCATTCTGTCCCATGCTGGCAATAATACC  
TTGTCAGCCCATACCCCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT  
GCCATATCAGAACACAAACCCCTGAAGAGGTTCTGATTTGATTTTTTTTTTTCTTCATGCC  
TACCCCTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTTGAT  
CAATTTTCATTCCCACCATTCGATTACAACCTCTAACTTAAATGGGTAACCCCTAAGGCATAT  
CAAAGAAGCAGATTGCATGATAAACGGAAATAGAAAAAAGAACCTACATTTATTTTGCTTT  
AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCCCTTTTTTACATTT  
TCGTATATTTATTTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT  
TGGAAGCTGAAAACCTGAATTTAAAGAATGCTATCTTGAAAATTGCATACGTCTGTGCAATT  
TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT  
TAATATCAAATTACAAAGTTTAGACTTGGAGGGAAATGGGCTTTTTAGAAAGCAAACAATTTT  
AAATATATTTTGTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT  
CCCACTTTGCAAACCTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTCATTGCTCA  
ATAATAAAGCCTGAATTCTGATCAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



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**FIGURE 288**

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKH  
SKRRVRDKDGD LKTQIEKLWT  
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDC  
ISKGGILVIPRNSDEINALQ  
DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRA  
QPNGGKRENCVLFSSQAQ GK  
WSDEACRSSKRYICEFTIPK

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**FIGURE 289**

GCGAGGACCGGGTATAAGAAGCCTCGTGGCCTTGCCCGGGCAGCCGCAGGTTCCCCGCGCGC  
CCCGAGCCCCCGCGCCATGAAGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCCTGCA  
GCTCCGCTGCTGCTTTCTTAGTGGGCTCGGCCAAGCCTGTGGCCCAGCCTGTCGCTGCGCTG  
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCTGGCCAACCCCTCGGCACCCTCAACCCGCT  
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACCACCTCATAGAGGGCTCCCAGAAGT  
GTGTGGCTGAGCTGGGTCCCCAGGCCGTGGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG  
GCCCTGACAGTGTTTGGCTGAGCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC  
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCTTCCCCGGCCCCCT  
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAA

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**FIGURE 290**

MKLAALLGLCVALSCSSAAAFVLGSAKPVAQPVAALESAAEAGAGTLANPLGTNLNPLKLLS  
SLGIPVNHLEGSQKCVAELGPQAVGAVKALKALLGALTVFG

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**FIGURE 291**

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT  
CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGTCCTCCTG  
GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCAGTCTCAGTCGCCAGAGACCCAGCCCC  
TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGG  
CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGGCAGCAGCTT  
GCCAAGGAGACTTCAAACCTTCGGATTACAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG  
CAACATGGTCTTCTCTCCATTTGGCATGTCTTGGCCATGACAGGCTTGATGCTGGGGGCCA  
CAGGGCCGACTGAAACCCAGATCAAGAGAGGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG  
CCCGGGCTCCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAAC  
GGGCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT  
TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCCTGCTATGAATTTTCGCAATGCCTCA  
CAGGCCAAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTTCCCAAAC  
GTTTGATGAGATTAATCCTGAAACCAAATTAATTCCTGTGGATTACATCTTGTTCAAAGGGA  
AATGGTTGACCCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTAC  
AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA  
TTTTCGTTGTATGTCCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCTCA  
TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA  
TGGCTCAGAAACATGAAAACCAGAAACATGGAAGTTTCTTTCCGAAGTTCAAGCTAGATCA  
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCCTTG  
CTGACCTTAGTGAACCTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA  
ACAGTGATTGAAGTTGATGAAAGGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTAC  
TGCTTATTCCATGCCCTCCTGTATCAAAGTGGACCGGCCATTTCAATTCATGATCTATGAAG  
AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTATAATTCAGG  
ACATGCATAAGCACTTCGTGCTGTAGTAGATGCTGAATCTGAGGTATCAAACACACACAGGA  
TACCAGCAATGGATGGCAGGGGAGAGTGTTCCTTTTGTTCTTAACAGTTTAGGGTGTCTC  
AAATAAATACAGTAGTCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC  
CTGAAACGGTGGACAGTGCTGAACCTTATATATATTTTTTCTACACATACATACCTATGAT  
AAAGTTTAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA  
TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACCTGATTATAGAGAAGGCTA  
CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAATTCA  
CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCCATCCCACTACTCAGAATGGCATGC  
TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTTCATTTAATGTTTTTGGACCATGGT  
TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA  
GCATTAAATTGATACATATTTTTTAAAAAAAAAAAAAAAAAAAA

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**FIGURE 292**

MKVVPSLLLSVLLAQVWLVPG LAPSPQSPETPAPQNTSRVVQAPREEEEDEQEASEEKAGE  
EEKAWLMASRQQLAKETS NFGFSLLRKISMRHDGNMVFS PFGMSLAMTGLMLGATGPTETQI  
KRG LHLQALKPTKPGL LPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF  
DTECVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLT PFD P  
VFTEVDTFHLDKYKTIKVPM MYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHL  
ALEDYLT TDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRI FSPFADLSELSA  
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF  
LGRVVNPTLL

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**FIGURE 293**

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGACATGAG  
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG  
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG  
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGTGTTCCC  
TGTCCAGAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAGGGCAGGGGCCCCA  
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCCTGAGTCCC  
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC  
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGGAGGAAGACCAAGACCACA  
TCTACCACCCCAGTAGGGCTCCAGGGGCCATCACTGCCCCCGCCCTGTCCCAAGGGCCAGG  
CTGTTGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCCAGCAGGCAAA  
AAAAAAAAAAAAAAAAA

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**FIGURE 294**

MRRLLLVTSLVVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL  
FPVQKPKLLTTEEKPRGQGGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE  
RPRLWVMPNHQVLLGPEEDQDHIYHPQ

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**FIGURE 295**

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG  
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGC  
TGTTTCTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAA  
TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC  
TAGTGCATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTATCTACCAGACCTTCT  
GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCATGAGAATGACATG  
CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC  
AGAGGGGGACGGCAACTGGGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG  
ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG  
CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC  
TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT  
ATGGAGAAGGAAAGTGTGGACTGACAACGGCCCCGGTGATCCCTGTGGTCTATGATTTTGGC  
GACGCCCAGAAAACAGCATCTTATTACTCACCTATGGCCAGCGGGAATTCACTGCGGGATT  
TGTTCA~~AG~~TTCAGGGTATTTAATAACGAGAGAGCAGCCAACGCCTTGTGTGCTGGAATGAGGG  
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT  
CCCCAGCAGTGTGGAGATTTTCTGGTTTTGATTGGAGTGGATATGGA~~ACT~~CATGTTGGTTA  
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTTTGTG  
GGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAACA~~ACT~~TACCCA  
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA



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**FIGURE 296**

MNQLSFLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN  
GVIIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG  
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI  
YQKYPVKYGEKGCWTDNGPVI PVVYDFGDAQKTASYYSPTYGQREFTAGFVQFRVFNNERAAAN  
ALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGTHVGYSRSSREITEAAVLL  
FYR

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**FIGURE 297**

GCGGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC  
CACGAGGCTGCCGCATCCTGCCCTCGGAACAATGGGACTCGGCGCGCGAGGTGCTTGGGCCG  
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCGCCCATGAAAGCGCAGCC  
ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACCTCCAGTGCTAACTCAAC  
AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC  
CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG  
GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC  
TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG  
TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACCTATGCAT  
TCTGAAGCAAAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAC  
GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC  
GGTATCGAACCATAGATGAACATGATGCCATCATTTAAGGAAATCCATGGACCAAGGATGGA  
ATACAGATTGATGCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCT  
CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA  
AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT  
TCATACAATGGTTTTAGCAAGTTCATAGTAAGACAAACAAGTCCTATCTTTTTTTTTTTGGCT  
GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA  
TGCCATCTGGGCATACAAATAAGAAGTTTGTACAGCACTCAGGATTTTGGGTATCTTTTGT  
AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA  
CAGAAATTATACAATCAAACCTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG  
TGCTTTAAACTGTAGTAGTTGGTCTAGAAACAAATACTCC

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**FIGURE 298**

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPNSSANSTETLQHVP  
SDH  
TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSV  
SQN  
TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSI  
LYIG  
CKMYYSRRGIRYRTIDEHDAII

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**FIGURE 299**

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG  
TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCAGCGATGGCGACCCTGTGGGGAGGC  
CTTCTTCGGCTTGGCTCCTTGCTCAGCCTGTCGTGCCTGGCGCTTCCGTGCTGCTGCTGGC  
GCAGCTGTCAGACGCCGCCAAGAATTTGAGGATGTCAGATGTAAATGTATCTGCCCTCCCT  
ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT  
CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA  
ATGCAAATATGAAGAAAGAAGCTCTGTACAATCAAGGTTACCATTATAATTTATCTCTCCA  
TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG  
CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT  
TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG  
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCCAAGAGCAGCGAAAGTCTGTCTTTGACCGG  
CATGTTGTCCTCAGCTAATTGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA  
CTGGAAAGAACTGACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTACCAACT  
GTTGCTGGAAGATTCAAACTGGAAGCAAAACTTGCTTGATTTTTTTTTCTTGTTAACGTA  
ATAATAGAGACATTTTTAAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCCTATTTG  
TGACTTTTACTAATAAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA  
AGCACTCTCTTTTTTACCACATAGTTTTAACTTGACTTTCAAGATAATTTTCAGGGTTTTTG  
TTGTTGTTGTTTTTTGTTTGTGTTGTTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGTT  
AACAACTTTTTTCAAGTCACTTTACTAAACAACTTTTGTAATAGACCTTACCTTCTATTT  
TCGAGTTTCATTTATATTTTGAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG  
ACTTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT  
CTAAATGCCTGGTGGCTTTTCACAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG  
CAATGCATCCTAGAACAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG  
GTGTGTGTGGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT  
TGCAATAAAGAAATTTTATTTTAAACCCAAGCCTCCCTGGATTGATAATATATACACATTTG  
TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT  
AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT  
TCTTCCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTTGAAACATCAA

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**FIGURE 300**

MATLWGGLRLGSLLSLCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENS  
GHYNNKIS  
QKDCDCLHVVEPMPVVRGPDVEAYCLRCECKYEERSSVTIKVTIIYLSILG  
LLLLYMYLTL  
VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLA  
RSRANVLNKVEYAQQRWKLQVQEQ  
RKSVFDRHVLS

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**FIGURE 301**

GCACCTGCGACCACCGTGAGCAGTC**ATG**GCGTACTCCACAGTGCAGAGAGTCGCTCTGGCTT  
CTGGGCTTGTCTGGCTCTGTCGCTGCTGCTGCCCCAAGGCCTTCCTGTCCCGCGGGAAGCGG  
CAGGAGCCGCCGCCGACACCTGAAGGAAAATTGGGCCGATTTCCACCTATGATGCATCATCA  
CCAGGCACCCTCAGATGGCCAGACTCCTGGGGCTCGTTTCCAGAGGTCTCACCTTGCCGAGG  
CATTTGCAAAGGCCAAAGGATCAGGTGGAGGTGCTGGAGGAGGAGGTAGTGGAAGAGGTCTG  
ATGGGGCAGATTATTCCAATCTACGGTTTTGGGATTTTTTTTATATATACTGTACATTCTATT  
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAAT**TGA**AAATCTAATATGGCGATAAAAA  
TCATTGTCTACATTAAAACTTCTTATAGTTCATAAAATTATTTCAAATCCATCATCTCTTTA  
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTTTCAGTTTACATAAGAATG  
TTTACTCAATGTTTAAGTGTTTTGCCCCAAAATTCACAATAACAAGGCAGAACTAGGACTT  
GAACATGGATCTTTTGTTCTTAATCCAGTGAGTGATACAATTCAATGCACTCCCCTGCCA

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**FIGURE 302**

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPPTPEGKLGRFPPMMHHHQAPSDGQT  
PGARFQRSHLAEAFKAKGSGGGAGGGGSGRGLMGQIIPYGFIFLYIILFKVSRILI  
ILHQ

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**FIGURE 303**

CGGCTCGAGTGCAGCTGTGGGGAGATTTTCAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTT  
GGATTTGAAAGTTGAGAGCAGCATGTTTTGCCCACTGAAACTCATCCTGCTGCCAGTGTTAC  
TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTG  
GGTGATTCAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT  
AGACTGGACTCTGTCACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA  
ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC  
AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA  
AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG  
AGGAGCCCAAAGAGCTCATGGTCCATGTGGGTGGATTGATTCAGATGGGATGTGTTTTCCAG  
AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA  
GGAGATTGTATTTCTTACTACCACAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG  
GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG  
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGAACCT  
GGTGTTCAGAAAACCATTTGTGCTGCATGTCAGCCCCGAAGAGCCTCGAACACTGGTGACCC  
CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTC  
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA  
GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG  
AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA  
CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA  
CCCAGTTTGGCCTTCTCTGAGGTCAGATCGGAACAACCTCACTTGAAAAAAGTCAGGTGGGG  
GAATGCCAAAAACACAGCAAGCCTTTTTGAGAAGAATGGAGAGTCCCTTCATCTCAGCAGCGG  
TGGAGACTCTCTCCTGTGTGTGTCCTGGGCCACTCTACCAGTGATTTTCAGACTCCCGCTCTC  
CCAGCTGTCTCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG  
CAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGC  
CTCTGGAGTGGGACACTGGCCCTGGGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCCGTT  
GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA  
AAACCAACCCAAATCAA



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**FIGURE 304**

MFCPLKLILLPVLLDYSGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG  
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES  
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY  
HKLMSVEYSQSWGHFQNRVNLVGDI FRNDGSIMLQGVRES DGGNYTCSIHLGNLVFKKTIV  
LHVSPEEPRTLVT PAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKT CGNKSSVNSTV  
LVKNTKKTNP EIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLR  
SDRNN SLEKSGGGMPKTQQAF

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**FIGURE 305**

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG  
GTTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGG  
AAACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCCATGCA  
GGATGAAGATGGATACATCACCTTAAATATTAAAACTCGGAAACCAGCTCTCGTCTCCGTTG  
GCCCTGCATCCTCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGG  
ATGGTTGTCGGGCTGGTGGCTCTGGGGATTTGGTCTGTTCATGCAGCGCAATTACCTACAAGA  
TGAGAATGAAAATCGCACAGGAAGCTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG  
TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCCTGTGACACAAAC  
TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTAACATGGGAAGAGAG  
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG  
AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT  
GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGAAGA  
TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG  
AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT  
TAATGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT  
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA

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**FIGURE 306**

MQDEDGYITLNIKTRKPALVSVGPASSSWVRVMALILLILCVGMVVGLVALGIWSVMQRNYL  
QDENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYGDSYGFRRHNLWE  
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEEFL  
EDGKGNMNCAYFHNGKMHPTFCENKHLYLMCERKAGMTKVDQLP

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**FIGURE 307**

CCCACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCCTGCCAGTCTCGCCCGCGATCCCGG  
CCCGGGGCTGTGGCGTCGACTCCGACCCAGGCAGCCAGCAGCCCGCGCGGGAGCCGGACCGC  
CGCCGGAGGAGCTCGGACGGCATGCTGAGCCCCCTCCTTTGCTGAAGCCCGAGTGCGGAGAA  
GCCCCGGGCAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAG  
CGGAGGAGAAGGAGGAGGAGGCGAACCCAGAGAGGGGCGAGCAAAAGAAGCGGTGGTGGTGGG  
CGTCGTGGCCATGGCGGCGGCTATCGCCAGCTCGCTCATCCGTCAGAAGAGGCAAGCCCGCG  
AGCGCGAGAAATCCAACGCCTGCAAGTGTGTGTCAGCAGCCCCAGCAAAGGCAAGACCAGCTGC  
GACAAAAACAAGTTAAATGTCTTTTCCCGGGTCAAACCTCTTCGGCTCCAAGAAGAGGCGCAG  
AAGAAGACCAGAGCCTCAGCTTAAGGGTATAGTTACCAAGCTATACAGCCGACAAGGCTACC  
ACTTGCAGCTGCAGGCGGATGGAACCATTGATGGCACCAAAGATGAGGACAGCACTTACACT  
CTGTTTAACCTCATCCCTGTGGGTCTGCGAGTGGTGGCTATCCAAGGAGTTCAAACCAAGCT  
GTACTTGGCAATGAACAGTGAGGGATACTTGTACACCTCGGAACTTTTCACACCTGAGTGCA  
AATTCAAAGAATCAGTGTTTGAAAATTATTATGTGACATATTCATCAATGATATACCGTCAG  
CAGCAGTCAGGCCGAGGGTGGTATCTGGGTCTGAACAAAGAAGGAGAGATCATGAAAGGCAA  
CCATGTGAAGAAGAACAAGCCTGCAGCTCATTTTCTGCCTAAACCACTGAAAGTGGCCATGT  
ACAAGGAGCCATCACTGCACGATCTCACGGAGTTCTCCCGATCTGGAAGCGGGACCCCAACC  
AAGAGCAGAAGTGTCTCTGGCGTGCTGAACGGAGGCAAATCCATGAGCCACAATGAATCAAC  
GTAGCCAGTGAGGGCAAAGAAGGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAAT  
TCTTCTAGCAGTCCTTCACCCAAAAGTTCAAATTTGTCAGTGACATTTACCAAACAAACAGG  
CAGAGTTCACTATTCTATCTGCCATTAGACCTTCTTATCATCCATACTAAAGC

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**FIGURE 308**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA28498

&gt;&lt;subunit 1 of 1, 245 aa, 1 stop

&gt;&lt;MW: 27564, pI: 10.18, NX(S/T): 1

MAAAIASSLIRQKRQAREREKSNACKCVSSPSKGKTSCDKNKLVFSRVKLFSGSKRRRRRP  
EPQLKGIVTKLYSRQGYHLQLQADGTIDGTKDEDSTYTLFNLIPVGLRVVAIQGVQTKLYLA  
MNSEGYLYTSELFPECKFKESVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVK  
KNKPAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKSRSVSGVLNGGKSMHNEST

**N-glycosylation site.**

amino acids 242-246

**Glycosaminoglycan attachment site.**

amino acids 165-169, 218-222

**Tyrosine kinase phosphorylation site.**

amino acids 93-100

**N-myristoylation site.**

amino acids 87-93, 231-237

**ATP/GTP-binding site motif A (P-loop).**

amino acids 231-239

**HBGF/FGF family proteins**

amino acids 78-94, 102-153

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**FIGURE 309**

CCAGGATGGAGCTGGGGCCTGTATAGCCATATTATTGTTCTATGCTACTAGACATGGGGGGG  
ACTTGGTGAAAAAGGTATTATCCAGCCAGAGGGTCTGGGAGCCCTGTCTTACTGAACCTGGG  
CAACCTGGATATTCTGAGACATATTTTGGGGGGATTTCAGTGAAAAAAGTGGGGGATCCCCT  
CCATTTAGAGTGTAGCAAAGGAAAAAACACCAAGGTTGGGTTTCCTTCCTGACATTGGCAGTG  
CCCCAGTAGGGGTGGGATGAGCGAATATTCCCAAAGCTAAAGTCCCACACCCTGTAGATTAC  
AAGAGTGGATTTGGCAGGAGTGTGCCCCAAAATACAGTGGAAAGGTGCCTGAAGATATTTAA  
ACCACGTCTTGGAAATTTAGTGGGTCTTGGCTTTGGGATAGGTGAAGTGAGGACAGACACTG  
GAGAGGAGGGAAAGGGGACGTTTTCAATAGGAGGCCAAACTCGAGGGTGGGATCCACTGAGG  
AGTACATAGGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCCACGGGTGGTAAGTGGCTGCT  
GTGGAGGGGGGTACGTGAGGGGGGGGTCTGGGGCTTATCCTCAGGTCCTGTGGGTGGGGCAG  
CGAGTCGGGGCCTGAGCGTCAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGGAGCCAG  
CGCGCTCCGGGCGCCTGCCGGTTTGGGGGTGTCTCCTCCCGGGGCGCTATGGCGGCGCTGGC  
CAGTAGCCTGATCCGGCAGAAGCGGGAGGTCCGCGAGCCCGGGGGCAGCCGGCCGGTGTCTGG  
CGCAGCGGCGCGTGTGTCCCCGCGGCACCAAGTCCCTTTGCCAGAAGCAGCTCCTCATCCTG  
CTGTCCAAGGTGCGACTGTGCGGGGGGCGGCCCGCGCGGCCGGACCGCGGGCCGGAGCCTCA  
GCTCAAAGGCATCGTCACCAAAGTGTCTGCCGCCAGGGTTTCTACCTCCAGGCGAATCCCG  
ACGGAAGCATCCAGGGCACCCCAGAGGATACCAGCTCCTTCACCCACTTCAACCTGATCCCT  
GTGGGCCTCCGTGTGGTCACCATCCAGAGCGCCAAGCTGGGTCACTACATGGCCATGAATGC  
TGAGGGACTGCTCTACAGTTCGCCGCATTTACAGCTGAGTGTCTGCTTTAAGGAGTGTGTCT  
TTGAGAATTACTACGTCTGTACGCCTCTGCTCTCTACCGCCAGCGTCGTTCTGGCCGGGCC  
TGGTACCTCGGCCTGGACAAGGAGGGCCAGGTCATGAAGGGAACCGAGTTAAGAAGACCAA  
GGCAGCTGCCCACTTTCTGCCCCAAGCTCCTGGAGGTGGCCATGTACCAGGAGCCTTCTCTCC  
ACAGTGTCCCCGAGGCCTCCCCTTCCAGTCCCCCTGCCCCCTTGAAATGTAGTCCCTGGACTG  
GAGGTTCCCTGCACTCCCAGTGAGCCAGCCACCACCACAACCTGT

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**FIGURE 310**

MAALASSLIRQKREVREPPGSRPVSAQRRVCPRGKSLCQKQLLILLSKVRLCGGRPARPDR  
GPEPQLKGIVTKLFCRQGFYQLQANPDGSIQGTPEDTSSFTHFNLIPVGLRVVTIQSAKLGHY  
MAMNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNR  
VKKTKAAAHFLPKLLEVAMYQEPSLHSVPEASPSSPPAP

**Tyrosine kinase phosphorylation site:**

amino acids 199-207

**N-myristoylation sites:**

amino acids 54-60, 89-95, 131-137

**HBGF/FGF family signature:**

amino acids 131-155

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**FIGURE 311**

**ATG**GCCGCGGCCATCGCTAGCGGCTTGATCCGCCAGAAGCGGCAGGCGCGGGAGCAGCACTG  
GGACCGGCCGTCTGCCAGCAGGAGGCGGAGCAGCCCCAGCAAGAACCGCGGGCTCTGCAACG  
GCAACCTGGTGGATATCTTCTCCAAAGTGC GCATCTTCGGCCTCAAGAAGCGCAGGTTGCGG  
CGCCAAGATCCCCAGCTCAAGGGTATAGTGACCAGGTTATATTGCAGGCAAGGCTACTACTT  
GCAAATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCT  
TCAACCTCATACCAGTGGGACTACGTGTTGTTGCCATCCAGGGAGTGAAAACAGGGTTGTAT  
ATAGCCATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTTACCCCTGAATGCAAGTT  
TAAAGAATCTGTTTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGG  
AATCTGGTAGAGCCTGGTTTTTGGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACAGA  
GTAAAGAAAACCAAACCAGCAGCTCATTTTCTACCCAAGCCATTGGAAGTTGCCATGTACCG  
AGAACCATCTTTGCATGATGTTGGGGAAACGGTCCC GAAGCCTGGGGTGACGCCAAGTAAAA  
GCACAAGTGC GTCTGCAATAATGAATGGAGGCAAACCAGTCAACAAGAGTAAGACAACA**TAG**



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**FIGURE 312**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA28503

&gt;&lt;subunit 1 of 1, 247 aa; 1 stop

&gt;&lt;MW: 27702, pI: 10.36, NX(S/T): 2

MAAAIASGLIRQKRQAREQHWD RPSASRRRSSPSKNRGLCNGNLVDIFSKVRIFGLKKRRLR  
RQDPQLKGIVTRLYCRQGYLQMHDPGALDGTKDDSTNSTLFNLI PVGLRVVAIQGVKTGLY  
IAMNGEGYLYPSELFTPECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNR  
VKKTKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKS KTT

**N-glycosylation site.**

amino acids 100-104, 242-246

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 28-32, 29-33

**Tyrosine kinase phosphorylation site.**

amino acids 199-207

**N-myristoylation site.**

amino acids 38-44, 89-95, 118-124, 122-128, 222-228

**HBGF/FGF family proteins.**

amino acids 104-155, 171-198

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**FIGURE 313**

GGGGAGAGGAATTGACCATGTAAAAGGAGACTTTTTTTTTTGGTGGTGGTGGCTGTTGGGTGCCTTGCAAAAAT  
GAAGGATGCAGGACGCAGCTTCTCCTGGAACCGAACGCAATGGATAAACTGATTGTGCAAGAGAGAAGGAAGA  
ACGAAGCTTTTTCTTGTGAGCCCTGGATCTTAACACAAATGTGTATATGTGCACACAGGGAGCATTCAAGAATG  
AAATAAACAGAGTTAGACCCGCGGGGGTTGGTGTGTTCTGACATAAATAAATAATCTTAAAGCAGCTGTTCCC  
CTCCCCACCCCCAAAAAAGGATGATTGGAATGAAGAACCGAGGATTCACAAAGAAAAAGTATGTTTCATTT  
TTCTCTATAAAGGAGAAAGTGAGCCAAGGAGATATTTTTGGAATGAAAAGTTTGGGGCTTTTTTAGTAAAGTAA  
AGAAGTGGTGTGGTGGTGTTCCTTTCTTTTTGAATTTCCCAAGAGGAGAGGAAATTAATAATACATCTGC  
AAAGAAATTTTCAAGAGAAGAAAAGTTGACCGCGGCAGATTGAGGCATTGATTGGGGGAGAGAAACAGCAGAGCA  
CAGTTGGATTTGTGCCTATGTTGACTAAAATTGACGGATAATTGCAGTTGGATTTTCTTCATCAACCTCCTTT  
TTTTTAAATTTTTATTCTTTTGGTATCAAGATCATGCGTTTTCTCTTGTCTTAACCACTGGATTTCCATCT  
GGATGTTGCTGTGATCAGTCTGAAATACAAGTGTGAATTCAGAAGGACCAACACCAGATAAATTATGAATG  
TTGAACAAGATGACCTTACATCCACAGCAGATAATGATAGTCTAGGTTTAACAGGGCCCTATTTGACCCCT  
GCTTGTGGTGTCTGGCTCTTCAACTTCTTGTGGTGGCTGGTCTGGTGCAGGCTCAGACCTGCCCTTCTGTGT  
GCTCCTGCAGCAACCAGTTCAGCAAGGTGATTTGTGTTGCGAAAAACCTGCGTGAGGTTCCGGATGGCATCTCC  
ACCAACACACGGCTGCTGAACCTCCATGAGAACCAATCCAGATCATCAAAGTGAACAGCTTCAAGCACTTGAG  
GCACTTGGAATCCTACAGTTGAGTAGGAACCATATCAGAACCATTGAAATTGGGGCTTCAATGGTCTGGCGA  
ACCTCAACACTCTGGAACCTTTGACAATCGTCTTACTACCATCCCGAATGGAGCTTTTGTATACTTGTCTAAA  
CTGAAGGAGCTCTGGTTGCGAAACAACCCCATTTGAAAGCATCCCTTCTTATGCTTTTAACAGAATTCCTTCTTT  
GCGCCGACTAGACTTAGGGGAATTGAAAAGACTTTCATACATCTCAGAAGGTGCCTTTGAAGGTCTGTCCAAT  
TGAGGTATTTGAACCTTGCCATGTGCAACCTTCGGGAAATCCCTAACCTCACACCGCTCATAAACTAGATGAG  
CTGGATCTTTCTGGGAATCATTTATCTGCCATCAGGCCTGGCTCTTCCAGGGTTTGATGCACCTTCAAAAAT  
GTGGATGATACAGTCCCAGATTCAAGTGATTGAACGGAATGCCTTTGACAACCTTCAGTCACTAGTGGAGATCA  
ACCTGGCACACAATAATCTAACATTACTGCCTCATGACCTTCTCACTCCCTTGATCATCTAGAGCGGATACAT  
TTACATCACAAACCTTGGAAGTGTAACTGTGACATACTGTGGCTCAGCTGGTGGATAAAAAGACATGGCCCCCTC  
GAACACAGCTTGTTGTGCCCCGTGTAACTCCTCCCAATCTAAAGGGGAGGTACATTGGAGAGCTCGACCAGA  
ATTACTTCACATGCTATGCTCCGGTGATTGTGGAGCCCCCTGCAGACCTCAATGTCACTGAAGGCATGGCAGCT  
GAGCTGAAATGTGCGGCCCTCCACATCCCTGACATCTGTATCTTGGATTACTCCAATGGAACAGTCATGACACA  
TGGGGCGTACAAAGTGGGATAGCTGTGCTCAGTGATGGTACGTTAAATTTACAAATGTAAGTGTGCAAGATA  
CAGGCATGTACACATGTATGGTGAGTAATCCGTTGGGAATACTACTGCTTCAGCCACCCTGAATGTTACTGCA  
GCAACCACTACTCCTTTCTTACTTTTCAACCGTCACAGTAGAGACTATGGAACCGTCTCAGGATGAGGCACG  
GACCACAGATAACAATGTGGGTCCCACTCCAGTGGTGCAGTGGGAGACCACCAATGTGACCACCTCTCTCACAC  
CACAGAGCACAAGGTCGACAGAGAAAACCTTCACCATCCCACTGACTGATATAAACAGTGGGATCCCAGGAATT  
GATGAGGTCATGAAGACTACCAAAATCATCATTGGGTGTTTTGTGGCCATCACACTCATGGCTGCAGTGATGCT  
GGTCATTTTCTACAAGATGAGGAAGCAGCACCATCGGCAAAACCATCACGCCCCAACAGGACTGTTGAAATTA  
TTAATGTGGATGATGAGATTACGGGAGACACACCCATGGAAAGCCACCTGCCATGCCTGCTATCGAGCATGAG  
CACCTAAATCACTATAACTCATACAAATCTCCCTTCAACCACACAACAACAGTTAACACAATAAATTCAATACA  
CAGTTCAGTGCATGAACCGTTATTGATCCGAATGAACTCTAAAGACAATGTACAAGAGACTCAAATCTAAACA  
TTTACAGAGTTACAAAAACAAACAATCAAAAAAAGACAGTTTATTAAAAATGACACAAATGACTGGGCTAA  
ATCTACTGTTTCAAAAAAGTGTCTTTACAAAAAACAAGAAAGAAATTTATTTATTAATAAATTCTATTG  
TGATCTAAAGCAGACAAAAA

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**FIGURE 314**

MLNKMTLHPQQIMIGPRFNRAFDPLLVLALLQLLVVAGLVRAQTCPSVCSCSNQFSKVIC  
VRKNLREVPDGI STNTRLLNLHENQIQI IKVNSFKHLRHLEILQLSRNHIRTIEIGAFNGLA  
NLNTLELFDNRLTTIPNGAFVYLSKLKELWLRNNPIESIPSYAFNRIPSLRRLDLGELKRLS  
YISEGAFEGLSNRLRYNLAMCNLREIPNLTPLIKLDLDELDSGNHLSAIRPGSFQGLMHLQKL  
WMIQSQIQVIERNAFDNLQSLVEINLAHNNLTLLPHDLFTPLHHLERIHLHHNPWNCNCDIL  
WLSWWIKDMAPSNTACCARCNTPPNLKGRYIGELDQNYFTCYAPVIVEPPADLNVTEGMAAE  
LKCRASSTLSVSWITPNGTVMTHGAYKVRIAVLSDGTNLNFTNVTVQDTGMYTCMVSNVSGN  
TTASATLNVTAATTTTFSYFSTVTVETMEPSQDEARTTDNNVGPTPVVDWETTNVTTSLTPQ  
STRSTEKFTTIPVTDINSGIPGIDEVMKTTKIIIGCFVAITLMAAVMLVIFYKMRKQHRQN  
HHAPTRTVEIINVDDIEITGDTPMESHLMPAIEHEHLNHYSYKSPFNHTTTVNTINSIHSS  
VHEPLLIRMNSKDNVQETQI

**Signal sequence:**

amino acids 1-44

**Transmembrane domain:**

amino acids 523-543

**N-glycosylation site.**amino acids 278-282, 364-368, 390-394, 412-416, 415-419,  
434-438, 442-446, 488-492, 606-610**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 183-187

**Casein kinase II phosphorylation site.**

amino acids 268-272, 417-421, 465-469, 579-583, 620-624

**N-myristoylation site.**amino acids 40-46, 73-79, 118-124, 191-197, 228-234, 237-243,  
391-397, 422-428, 433-439, 531-537

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**FIGURE 315**

GCGCCGGGAGCCCATCTGCCCCCAGGGGCACGGGGCGCGGGGCCGGCTCCCGCCCCGGCACAT  
GGCTGCAGCCACCTCGCGCGCACCCCGAGGCGCGCGCCAGCTCGCCCGAGGTCCGTCGGA  
GGCGCCCCGGCGCCCCGGAGCCAAGCAGCAACTGAGCGGGGAAGCGCCCGCTCCGGGGATC  
GGGATGTCCCTCCTCCTTCTCCTCTTGCTAGTTTCTACTATGTTGGAACCTTGGGGACTCA  
CACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACTTTGGCCTGCCACCATCAACTGGGGC  
TTCCAGAAAAAGACACTCTGGATATTGAATGGCTGCTCACCGATAATGAAGGGAACCAAAAA  
GTGGTGATCACTTACTCCAGTCGTCATGTCTACAATAACTTGACTGAGGAACAGAAGGGCCG  
AGTGGCCTTTGCTTCCAATTTCTTGGCAGGAGATGCCTCCTTGCAAGATTGAACCTCTGAAGC  
CCAGTGATGAGGGCCGGTACACCTGTAAGGTTAAGAATTGAGGCGCTACGTGTGGAGCCAT  
GTCATCTTAAAAGTCTTAGTGAGACCATCCAAGCCCAAGTGTGAGTTGGAAGGAGAGCTGAC  
AGAAGGAAGTGACCTGACTTTGCAAGTGTGAGTCATCCTCTGGCACAGAGCCCATTGTGTATT  
ACTGGCAGCGAATCCGAGAGAAAGAGGGAGAGGATGAACGTCTGCCTCCCAAATCTAGGATT  
GACTACAACCACCCTGGACGAGTTCTGCTGCAGAATCTTACCATGTCCTACTCTGGACTGTA  
CCAGTGCACAGCAGGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCGAGTAAGTGTACAGT  
ATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTG  
ATTTTCCTCTTGGTGTGGCTGCTAATCCGAAGGAAAGACAAAGAAAGATATGAGGAAGAAGA  
GAGACCTAATGAAATTCGAGAAGATGCTGAAGCTCCAAAAGCCCGTCTTGTGAAACCCAGCT  
CCTCTTCCTCAGGCTCTCGGAGCTCACGCTCTGGTTCTTCTCCTCCACTCGCTCCACAGCAAAT  
AGTGCCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGGCCAC  
CCAGGCATACAGCCTAGTGGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATG  
CTAATCTGACCAAAGCAGAAACCACACCCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAA  
ACGGTCTGGAATTACAATGGACTTGACTCCCACGCTTTCCTAGGAGTCAGGGTCTTTGGACTC  
TTCTCGTCATTGGAGCTCAAGTCACCAGCCACACAACCAGATGAGAGGTCATCTAAGTAGCA  
GTGAGCATTGCACGGAACAGATTGAGATGAGCATTTCCTTATACAATACCAAACAAGCAAA  
AGGATGTAAGCTGATTGATCTGTAAAAAGGCATCTTATTGTGCCTTTAGACCAGAGTAAGGG  
AAAGCAGGAGTCCAAATCTATTTGTTGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTG  
AGGTGAATATACCTAAACTTTTAATGTGGGATATTTTGTATCAGTGCTTTGATTACAAATT  
TTCAAGAGGAAATGGGATGCTGTTTGTAAATTTTCTATGCATTTCTGCAAACTTATTGGATT  
ATTAGTTATTGAGACAGTCAAGCAGAACCCACAGCCTTATTACACCTGTCTACACCATGTAC  
TGAGCTAACCCTTCTAAGAACTCCAAAAAGGAAACATGTGTCTTCTATTCTGACTTAAC  
TTCATTTGTCATAAGGTTTGGATATTAATTTCAAGGGGAGTTGAAATAGTGGGAGATGGAGA  
AGAGTGAATGAGTTTCTCCCACTCTATACTAATCTCACTATTTGTATTGAGCCCAAAATAAC  
TATGAAAGGAGACAAAATTTGTGACAAAGGATTGTGAAGAGCTTTCATCTTCATGATGTT  
ATGAGGATTGTTGACAAACATTAGAAATATATAATGGAGCAATTGTGGATTTCCTCCTCAAT  
CAGATGCCTCTAAGGACTTTCTGCTAGATATTTCTGGAAGGAGAAAATACAACATGTCATT  
TATCAACGTCCTTAGAAAGAATTCCTCTAGAGAAAAAGGGATCTAGGAATGCTGAAAGATTA  
CCCAACATACCATTATAGTCTCTTCTTTCTGAGAAAAATGTGAAACCAGAATTGCAAGACTGG  
GTGGACTAGAAAGGAGATTAGATCAGTTTTCTCTTAATATGTCAAGGAAGGTAGCCGGGCA  
TGGTGCCAGGCACCTGTAGGAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCC  
ATTGCACTCCAGCCTGGGTGACAGAGCGGGACTCCGTCTC

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**FIGURE 316**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45419

&gt;&lt;subunit 1 of 1, 373 aa, 1 stop

&gt;&lt;MW: 41281, pI: 8.33, NX(S/T): 3

MSLLLLLLVSYYVGTLGTHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKV  
VITYSSRHVYNNLTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHV  
ILKVLVRPSKPKCELEGELTEGSDLTQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRID  
YNHPGRVLLQNLTMSYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLI  
FLLVWLLIRRKDKERYEEEEERPNEIREDAEAPKARLVKPSSSSSGSRSSSRSGSSSTRSTANS  
ASRSQRTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHANLTKAETTPSMIPSQSRAFQTV

**Signal sequence:**

amino acids 1-16

**Transmembrane domain:**

amino acids 232-251

FIGURE 317

[illegible]

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**FIGURE 318**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA82361

&gt;&lt;subunit 1 of 1, 352 aa, 1 stop

&gt;&lt;MW: 38938, pI: 7.86, NX(S/T): 3

MALLLCFVLLCGVVDFARSL SITTP EEMIEKAKGETAYLPCKFTLSPEDQGPLDIEWLISPA  
DNQKVDQVIILYSGDKIYDDYYPDLKGRVHFTSNDLKS GDASINVTNLQLSDIGTYQCKVKK  
APGVANKKIHLVVLVKPSGARC YVDGSEEIGSDFKIKCEPKESLPLQYEWQKLSDSQKMPT  
SWLAEMTSSVISVKNASSEYSGTYSCTVRNRVGS DQCLLRNLNVPPSNKAGLIAGAIIGTLL  
ALALIGLIIFCCRKKRREEKYEKEVHHDIREDVPPPKSRTSTARSYIGSNHSSLGSMSPSNM  
EGYSKTQYNQVPSEDFERTPQSPTLPPAKFKYPYKTDGITVV

**Signal sequence.**

amino acids 1-19

**Transmembrane domain:**

amino acids 236-257

**N-glycosylation sites.**

amino acids 106-110, 201-205, 298-302

**Tyrosine kinase phosphorylation sites.**

amino acids 31-39, 78-85, 262-270

**N-myristoylation sites.**amino acids 116-122, 208-214, 219-225, 237-243, 241-247,  
245-251, 296-302**Myelin P0 protein.**

amino acids 96-125

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**FIGURE 319**

TGAAATGACTTCCACGGCTGGGACGGGAACCTTCCACCCACAGCTATGCCTCTGATTGGTGA  
ATGGTGAAGGTGCCTGTCTAACTTTTCTGTAAAAAGAACCAGCTGCCTCCAGGCAGCCAGCC  
CTCAAGCATCACTTACAGGACCAGAGGGACAAGACATGACTGTGATGAGGAGCTGCTTTTCGC  
CAATTTAACACCAAGAAGAATTGAGGCTGCTTGGGAGGAAGGCCAGGAGGAACACGAGACTG  
AGAGATGAATTTTCAACAGAGGCTGCAAAGCCTGTGGACTTTAGCCAGACCCTTCTGCCCTC  
CTTTGCTGGCGACAGCCTCTCAAATGCAGATGGTTGTGCTCCCTTGCCTGGGTTTTACCCTG  
CTTCTCTGGAGCCAGGTATCAGGGGCCCAGGGCCAAGAATTCCACTTTGGGCCCTGCCAAGT  
GAAGGGGGTTGTTCCCCAGAACTGTGGGAAGCCTTCTGGGCTGTGAAAGACACTATGCAAG  
CTCAGGATAACATCAGAGTGCCCGGCTGCTGCAGCAGGAGGTTCTGCAGAACGTCTCGGAT  
GCTGAGAGCTGTTACCTTGTCCACACCCTGCTGGAGTTCTACTTGAAAAGTGTTCACAAAA  
CCACCACAATAGAACAGTTGAAGTCAGGACTCTGAAGTCATTCTCTACTCTGGCCAACAAC  
TTGTTCTCATCGTGTCAAACTGCAACCCAGTCAAGAAAATGAGATGTTTTCCATCAGAGAC  
AGTGCACACAGGCGGTTTCTGCTATTCCGGAGAGCATTCAAACAGTTGGACGTAGAAGCAGC  
TCTGACCAAAGCCCTTGGGGAAGTGGACATTCTTCTGACCTGGATGCAGAAATTCTACAAGC  
TCTTGAATGTCTAGACCAGGACCTCCCTCCCCCTGGCACTGGTTTGTTCCTGTGTCATTTCA  
AACAGTCTCCCTTCCTATGCTGTTCACTGGACACTTCACGCCCTTGGCCATGGGTCCCATTC  
TTGGCCCAGGATTATTGTCAAAGAAGTCATTCTTTAAGCAGCGCCAGTGACAGTCAGGGAAG  
GTGCCTCTGGATGCTGTGAAGAGTCTACAGAGAAGATTCTTGTATTTATTACAACCTCTATTT  
AATTAATGTCAGTATTTCAACTGAAGTTCTATTTATTTGTGAGACTGTAAGTTACATGAAGG  
CAGCAGAATATTGTGCCCCATGCTTCTTTACCCCTCACAATCCTTGCCACAGTGTGGGGCAG  
TGGATGGGTGCTTAGTAAGTACTTAATAAACTGTGGTGCTTTTTTTGGCCTGTCTTTGGATT  
GTTAAAAAACAGAGAGGGATGCTTGGATGTAAACTGAACTTCAGAGCATGAAAATCACACT  
GTCTTCTGATATCTGCAGGGACAGAGCATTGGGGTGGGGGTAAGGTGCATCTGTTTGAAAAG  
TAAACGATAAAATGTGGATTAAAGTGCCCAGCACAAAGCAGATCCTCAATAAACATTTTCATT  
TCCCACCCACACTCGCCAGCTCACCCCATCATCCCTTCCCTTGGTGCCCTCCTTTTTTTTTT  
TATCCTAGTCATTCTTCCCTAATCTTCCACTTGAGTGTCAAGCTGACCTTGCTGATGGTGAC  
ATTGCACCTGGATGTACTATCCAATCTGTGATGACATTCCCTGCTAATAAAAGACAACATAA  
CTCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



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**FIGURE 320**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA88002

&gt;&lt;subunit 1 of 1, 206 aa, 1 stop

&gt;&lt;MW: 23799, pI: 9.12, NX(S/T): 3

MNFQQRLQSLWTLARPFPCPLLATASQMVMVLPCLGFTLLLWSQVSGAQGGQEFHFGPCQVK  
GVVPQKLWEAFWAVKDTMQAQDNITSARLLQQEVLQNVSDAESCYLVTLLLEFYLKTVFKNH  
HNRTVEVRTLKSFSTLANNFVLIVSQLQPSQENEMFSIRDSAHRRFLLFRRAFKQLDVEAAL  
TKALGEVDILLTWMQKFYKL

**Signal sequence:**

amino acids 1-42

**N-glycosylation sites.**

amino acids 85-89, 99-103, 126-130

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**FIGURE 321**

AAGGAGCAGCCCGCAAGCACCAAGTGAGAGGCATGAAGTTACAGTGTGTTTCCCTTTGGCTC  
CTGGGTACAATACTGATATTGTGCTCAGTAGACAACCACGGTCTCAGGAGATGTCTGATTTC  
CACAGACATGCACCATATAGAAGAGAGTTTCCAAGAAATCAAAGAGCCATCCAAGCTAAGG  
ACACCTTCCCAAATGTCACTATCCTGTCCACATTGGAGACTCTGCAGATCATTAAAGCCCTTA  
GATGTGTGCTGCGTGACCAAGAACCTCCTGGCGTTCTACGTGGACAGGGTGTTCAAGGATCA  
TCAGGAGCCAAACCCCAAATCTTGAGAAAAATCAGCAGCATTGCCAACTCTTTCCTCTACA  
TGCAGAAAACCTCTGCGGCAATGTCAGGAACAGAGGCAGTGTCACTGCAGGCAGGAAGCCACC  
AATGCCACCAGAGTCATCCATGACAACTATGATCAGCTGGAGGTCCACGCTGCTGCCATTAA  
ATCCCTGGGAGAGCTCGACGTCTTCTAGCCTGGATTAATAAGAATCATGAAGTAATGTTCT  
CAGCTTGATGACAAGGAACCTGTATAGTGATCCAGGGATGAACACCCCCTGTGCGGTTTACT  
GTGGGAGACAGCCACCTTGAAGGGGAAGGAGATGGGGAAGGCCCTTGCAGCTGAAAGTCC  
CACTGGCTGGCCTCAGGCTGTCTTATTCCGCTTGAAAATAGGCAAAAAGTCTACTGTGGTAT  
TTGTAATAAACTCTATCTGCTGAAAGGGCCTGCAGGCCATCCTGGGAGTAAAGGGCTGCCTT  
CCCATCTAATTTATTGTAAAGTCATATAGTCCATGTCTGTGATGTGAGCCAAGTGATATCCT  
GTAGTACACATTGTACTGAGTGTTTTTCTGAATAAATTCCATATTTTACCTATGA

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**FIGURE 322**

></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92282

><subunit 1 of 1; 177 aa, 1 stop

><MW: 20452, pI: 8.00, NX(S/T): 2

MKLQCVSLWLLGTILILCSVDNHGLRRCLISTDMHHIEESFQEIKRAIQAKDTFPNVTILST

LETLQIIKPLDVCCVTKNLLAFYVDRVFKDHQEPNPKILRKISSIANSFLYMQKTLRQCQEQ

RQCHCRQEATNATRVIHNYDQLEVHAAAIKSLGELDVFLAWINKNHEVMFSA

**Signal sequence:**

amino acids 1-18

**N-glycosylation sites.**

amino acids 56-60, 135-139

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 102-106

**N-myristoylation site.**

amino acids 24-30

**Actinin-type actin-binding domain signature 1.**

amino acids 159-169

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**FIGURE 323**

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACTTGGCTTCGTTAG  
AACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACACTAT  
AGAATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAAGTGCACCTC  
GGTTCTATCGATAATCTCAGCACCAGCCACTCAGAGCAGGGCACGATGTTGGGGGCCCCGCCT  
CAGGCTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCATGAGCGTCCTCAGAGCCTATCCCA  
ATGCCTCCCCACTGCTCGGCTCCAGCTGGGGTGGCCTGATCCACCTGTACACAGCCACAGCC  
AGGAACAGCTACCACCTGCAGATCCACAAGAATGGCCATGTGGATGGCGCACCCCATCAGAC  
CATCTACAGTGCCCTGATGATCAGATCAGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGA  
TGAGCAGAAGATACCTCTGCATGGATTTTCAGAGGCAACATTTTTGGATCACACTATTTTCGAC  
CCGGAGAACTGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCC  
TCAGTATCACTTCCTGGTCAGTCTGGGCCGGGCGAAGAGAGCCTTCTGCTGCCAGGCATGAACC  
CACCCCCGTACTCCCAGTTCCTGTCCCGGAGGAACGAGATCCCCCTAATTCATTCAACACC  
CCCATACCACGGCGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCCTGAACGT  
GCTGAAGCCCCGGGCCCCGGATGACCCCGGCCCCGGCCTCCTGTTTACAGGAGCTCCCGAGCG  
CCGAGGACAACAGCCCGATGGCCAGTGACCCATTAGGGGTGGTCAGGGGCGGTTCGAGTGAAC  
ACGCACGCTGGGGGAACGGGCCCCGGAAGGCTGCCGCCCTTCGCCAAGTTCATCTAGGGTCTG  
CTGG

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**FIGURE 324**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA142238

&gt;&lt;subunit 1 of 1, 251 aa, 1 stop

&gt;&lt;MW: 27954, pI: 9.22, NX(S/T): 1

MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSWGGLIHLYTATARNSYHLQIHKNGHVD  
GAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNI FGSHYFDPENCRFQHQTLENGY  
DVIHSPQYHFLVSLGRAKRAFLPGMNPPYPYSQFLSRNEIPLIHFNTPIPRRHTRSAEDDSE  
RDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNT HAGGTGPEGCRPFA  
KFI

**Important features of the protein:****Signal peptide:**

amino acids 1-24

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 175-179

**N-myristoylation site.**

amino acids 33-39, 100-106, 225-231, 229-235

**HBGF/FGF family proteins**

amino acids 73-124

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**FIGURE 325**

GGAAAAGGTACCCGCGAGAGACAGCCAGCAGTTCTGTGGAGCAGCGGTGGCCGGCTAGG**ATG**  
GGCTGTCTCTGGGGTCTGGCTCTGCCCCCTTTCTTCTTCTGCTGGGAGGTTGGGGTCTCTGG  
GAGCTCTGCAGGCCCCAGCACCCGCGAGAGCAGACACTGCGATGACAACGGACGACACAGAAG  
TGCCCGCTATGACTCTAGCACCGGGCCACGCCGCTCTGGAACTCAAACGCTGAGCGCTGAG  
ACCTCTTCTAGGGCCTCAACCCAGCCGGCCCCATTCCAGAAGCAGAGACCAGGGGAGCCAA  
GAGAATTTCCCCTGCAAGAGAGACCAGGAGTTTCACAAAACATCTCCCACTTCATGGTG  
TGATCGCCACCTCCGTGGAGACATCAGCCGCCAGTGGCAGCCCCGAGGGAGCTGGAATGACC  
ACAGTTCAGACCATCACAGGCAGTGATCCCGAGGAAGCCATCTTTGACACCCTTTGCACCGA  
TGACAGCTCTGAAGAGGCAAAGACACTCACAATGGACATATTGACATTGGCTCACACCTCCA  
CAGAAGCTAAGGGCCTGTCCTCAGAGAGCAGTGCCCTCTTCCGACGGCCCCCATCCAGTCATC  
ACCCCGTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCC  
GTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCCGTCAT  
GGTCCCCGGGATCTGATGTCACTCTCCTCGCTGAAGCCCTGGTGACTGTCACAAACATCGAG  
GTTATTAATTGCAGCATCACAGAAATAGAAACAACAACTTCCAGCATCCCTGGGGCCTCAGA  
CATAGATCTCATCCCCACGGAAGGGGTGAAGGCCTCGTCCACCTCCGATCCACCAGCTCTGC  
CTGACTCCACTGAAGCAAACACACATCACTGAGGTCACAGCCTCTGCCGAGACCCTGTCC  
ACAGCCGGCACACAGAGTCAGCTGCACCTCATGCCACGGTTGGGACCCCCACTCCCCACTAA  
CAGCGCCACAGAAAGAGAAGTGACAGCACCCGGGGCCACGACCCTCAGTGGAGCTCTGGTCA  
CAGTTAGCAGGAATCCCCTGGAAGAAACCTCAGCCCTCTCTGTTGAGACACCAAGTTACGTC  
AAAGTCTCAGGAGCAGCTCCGGTCTCCATAGAGGCTGGGTGAGCAGTGGGCAAAACAACCTC  
CTTTGCTGGGAGCTCTGCTTCCTCCTACAGCCCCTCGGAAGCCGCCCTCAAGAACTTCACCC  
CTTCAGAGACACCGACCATGGACATCGCAACCAAGGGGCCCTTCCCCACCAGCAGGGACCCT  
CTTCCTTCTGTCCCTCCGACTACAACCAACAGCAGCCGAGGGACGAACAGCACCTTAGCCAA  
GATCACAACTCAGCGAAGACCACGATGAAGCCCCAACAGCCACGCCCACGACTGCCCGGAC  
GAGGCCGACCACAGACG**TGAG**TGCAGGTGAAAATGGAGGTTTCCTCCTCCTGCGGCTGAGTG  
TGGCTTCCCCGGAAGACCTCACTGACCCCAGAGTGGCAGAAAGGCTGATGCAGCAGCTCCAC  
CGGGAACCTCCACGCCCACGCGCCTCACTTCCAGGTCTCCTTACTGCGTGTCAGGAGAGGCTA  
ACGGACATCAGCTGCAGCCAGGCATGTCCCGTATGCCAAAAGAGGGTGCTGCCCCTAGCCTG  
GGCCCCCACCAGACAGACTGCAGCTGCGTTACTGTGCTGAGAGGTACCCAGAAGGTTCCCATG  
AAGGGCAGCATGTCCAAGCCCCTAACCCAGATGTGGCAACAGGACCCTCGCTCACATCCAC  
CGGAGTGTATGTATGGGAGGGGCTTACCTGTTCCAGAGGTGTCCTTGGACTCACCTTGG  
CACATGTTCTGTGTTTCAGTAAAGAGAGACCTGATCACCCATCTGTGTGCTTCCATCCTGCA  
TTAAATTCACCTCAGTGTGGCCCAAAAAA

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**FIGURE 326**

MGCLWGLALPLFFFCWEVGVSGSSAGPSTRRADTAMTTDDTEVPAMTLAPGHAALETQTL  
ETSSRASTPAGPIPEAETRGAKRISPAETRSFTKTSPNFMVLIATSVETSAASGSPEGAGM  
TTVQTTITGSDPEEAI FDTLCTDDSSSEEAKTLTMDILT LAHTSTEAKGLSSESSASSDGPHV  
ITPSRASESSASSDGPHPVITPSRASESSASSDGPHPVITPSWSPGSDVTLLAEALVTVTNI  
EVINCSITEIETTTSSIPGASDIDLIPTEGVKASSTSDPPALPDSTEAKPHITEVTASAETL  
STAGTTESAAPHATVGTPLPTNSATEREVTAPGATTL SGALVTVSRNPLEETSALSVETPSY  
VKVSGAAPVSIEAGSAVGKTTSFAGSSASSYSPEAALKNFTPSETPTMDIATKGPFPTSRD  
PLPSVPPTTTNSSRGTNSTLAKITTS AKTTMKPQQPRPRLPGRGRPQT

**N-glycosylation sites:**

amino acids 252-256, 445-449, 451-455

**cAMP-and cGMP-dependent protein kinase phosphorylation site.**

amino acids 84-90

**Casein kinase II phosphorylation sites.**amino acids 37-41, 108-112, 131-135, 133-137, 148-152, 165-169,  
246-250, 254-258, 256-260, 269-273, 283-287, 333-337, 335-339,  
404-408, 414-418, 431-435**N-myristoylation sites.**amino acids 2-8, 19-25, 117-123, 121-127, 232-238, 278-284, 314-  
320, 349-355, 386-392, 397-403, 449-455**ATP/GTP-binding site motif A (P-loop).**

amino acids 385-393

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**FIGURE 327**

GCGGAGCATCCGCTGCGGTCCTCGCCGAGACCCCCGCGCGGATTCGCCGGTCCTTCCCGCGG  
GCGCGACAGAGCTGTCCTCGCACCTGGATGGCAGCAGGGGCGCCGGGGTCTCTCGACGCCA  
GAGAGAAATCTCATCATCTGTGCAGCCTTCTTAAAGCAAACCTAAGACCAGAGGGAGGATTAT  
CCTTGACCTTTGAAGACCAAACTAACTGAAATTTAAATGTTCTTCGGGGGAGAAGGGAG  
CTTGACTTACACTTTGGTAATAATTTGCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATT  
GCCTCAAAAAGAGTCTAGAAGATGTTGTCATTGACATCCAGTCATCTCTTTCTAAGGGAATC  
AGAGGCAATGAGCCCGTATATACTTCAACTCAAGAAGACTGCATTAATTCTTGCTGTTCAAC  
AAAAACATATCAGGGGACAAAGCATGTAACCTGATGATCTTCGACACTCGAAAAACAGCTA  
GACAACCCAACTGCTACCTATTTTTCTGTCCCAACGAGGAAGCCTGTCCATTGAAACCAGCA  
AAAGGACTTATGAGTTACAGGATAATTACAGATTTTCCATCTTTGACCAGAAATTTGCCAAG  
CCAAGAGTTACCCAGGAAGATTCTCTCTTACATGGCCAATTTTCAAGCAGTCACTCCCC  
TAGCCCATCATCACACAGATTATTCAAAGCCCACCGATATCTCATGGAGAGACACACTTTCT  
CAGAAGTTTGGATCCTCAGATCACCTGGAGAACTATTTAAGATGGATGAAGCAAGTGCCCA  
GCTCCTTGCTTATAAGGAAAAAGGCCATTCTCAGAGTTCACAATTTTCTCTGATCAAGAAA  
TAGCTCATCTGCTGCCTGAAAATGTGAGTGCCTCCAGCTACGGTGGCAGTTGCTTCTCCA  
CATAACACCTCGGCTACTCCAAAGCCCCGCCACCCTTCTACCCACCAATGCTTCAGTGACACC  
TTCTGGGACTTCCAGCCACAGCTGGCCACCACAGCTCCACCTGTAACCACTGTCACTTCTC  
AGCCTCCCACGACCCTCATTTCTACAGTTTTTACACGGGCTGCGGCTACACTCCAAGCAATG  
GCTACAACAGCAGTTCTGACTACCACCTTTCAGGCACCTACGGACTCGAAAGGCAGCTTAGA  
AACCATACCGTTTACAGAAATCTCCAACCTTAACTTTGAACACAGGGAATGTGTATAACCCTA  
CTGCACTTTCTATGTCAAATGTGGAGTCTTCCACTATGAATAAACTGCTTCCTGGGAAGGT  
AGGGAGGCCAGTCCAGGCAGTTCCTCCAGGGCAGTGTTCCAGAAAATCAGTACGGCCTTCC  
ATTTGAAAAATGGCTTCTTATCGGGTCCCTGCTCTTTGGTGTCTGTTCTGCTGATAGGCC  
TCGTCTCCTGGGTAGAATCCTTTCCGAATCACTCCGCAGGAAACGTTACTCAAGACTGGAT  
TATTTGATCAATGGGATCTATGTGGACATCTAAGGATGGAACCTCGGTGTCTCTTAATTCATT  
TAGTAACCAGAAGCCCAAATGCAATGAGTTTCTGCTGACTTGCTAGTCTTAGCAGGAGGTTG  
TATTTTGAAGACAGGAAAATGCCCCCTTCTGCTTTCTTTTTTTTTTTGGAGACAGAGTCTT  
GCTCTGTTGCCAGGCTGGAGTGAGTAGCACGATCTCGGCTCTCACCGCAACCTCCGTCTC  
CTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTAAGTATCTGGGATTACAGGCATGTGCCA  
CCACACCTGGGTGATTTTTGTATTTTTAGTAGAGACGGGGTTTCACCATGTTGGTCAGGCTG  
GTCTCAAACCTCCTGACCTAGTGATCCACCCTCCTCGGCCTCCCAAAGTGCTGGGATTACAGG  
CATGAGCCACCACAGCTGGCCCCCTTCTGTTTTATGTTTGGTTTTTGAGAAAGGAATGAAGTG  
GGAACCAAATTAGGTAATTTTGGGTAATCTGTCTCTAAAATATTAGCTAAAAACAAAGCTCT  
ATGTAAAGTAATAAAGTATAATTGCCATATAAATTTCAAATTCAACTGGCTTTTATGCAAA  
GAAACAGGTTAGGACATCTAGGTTCCAATTCATTACATTCTTGGTTCCAGATAAAATCAAC  
TGTTTATATCAATTTCTAATGGATTTGCTTTTCTTTTTATATGGATTCTTTAAACTTATT  
CCAGATGTAGTTCCCTTCCAATTAAATATTTGAATAAATCTTTTGTACTCAA



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**FIGURE 328**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45410.

&gt;&lt;subunit 1 of 1, 431 aa, 1 stop

&gt;&lt;MW: 46810, pI: 6.45, NX(S/T): 6

MFFGGEGSLTYTLVVICFLTLRLSASQNCLKKSLEDVVIDIQSSLSKGIRGNEPVYTSTQED  
CINSCCSTKNISGDKACNLMI F DTRKTRARQPN CYLFFCPNEEACPLKPAKGLMSYRIITDFP  
SLTRNLPSQELPQEDSLLHGQFSQAVTPLAHHHTDYSKPTDISWRDTLSQKFGSSDHLEKLF  
KMDEASAQLLAYKEKGHSQSSQFSSDQEI A HLLPENVSALPATVAVASPH TTSATPKPATLL  
PTNASVTPSGTSQPQLATTAPPVTTVTSQPPTTLISTVFTRAAATLQAMATTAVLTTTFQAP  
TDSKGSLETIPFTEISNLT LNTGNVYNPTALSMSNVESSTMNKTASWEGREASPGSSSQGSV  
PENQYGLPF EKWLLIGSLLFGVLFLVIGLVLLGRILSESLRRKRYSR LDYLINGIYVDI

**Signal sequence.**

amino acids 1-25

**Transmembrane domain.**

amino acids 384-405

**N-glycosylation sites.**

amino acids 72-76, 222-226, 251-255, 327-331, 352-356

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 415-419

**Tyrosine kinase phosphorylation site.**

amino acids 50-57

**N-myristoylation sites.**

amino acids 4-10, 48-54, 315-321

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**FIGURE 329**

CTCCACGGTGTCCAGCGCCCAGAAATGCGGCTTCTGGTCCTGCTATGGGGTTGCCTGCTGCT  
CCCAGGTTATGAAGCCCTGGAGGGCCCAGAGGAAATCAGCGGGTTCGAAGGGGACACTGTGT  
CCCTGCAGTGCACCTACAGGGAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGT  
GGGATCCTCTTCTCTCGCTGCTCTGGCACCATCTATGCAGAAGAAGAAGGCCAGGAGACAAT  
GAAGGGCAGGGTGTCCATCCGTGACAGCCGCCAGGAGCTCTCGCTCATTGTGACCCTGTGGA  
ACCTCACCTGCAAGACGCTGGGGAGTACTGGTGTGGGGTCGAAAAACGGGGCCCCGATGAG  
TCTTTACTGATCTCTCTGTTCTGTTCTTCCAGGACCCTGCTGTCCTCCCTCCCCTTCTCCCAC  
CTTCCAGCCTCTGGCTACAACACGCCTGCAGCCCAAGGCAAAAGCTCAGCAAACCCAGCCCC  
CAGGATTGACTTCTCCTGGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGG  
GCTGAGGGCCCTCCATTGCCAGGGACTTCCAGTACGGGCACGAAAGGACTTCTCAGTACAC  
AGGAACCTCTCCTCACCCAGCGACCTCTCCTCCTGCAGGGAGCTCCCGCCCCCCCATGCAGC  
TGGACTCCACCTCAGCAGAGGACACCAGTCCAGCTCTCAGCAGTGGCAGCTCTAAGCCCAGG  
GTGTCCATCCCGATGGTCCGCATACTGGCCCCAGTCTGGTGTGCTGAGCCTTCTGTGAGC  
CGCAGGCCTGATCGCCTTCTGCAGCCACCTGCTCCTGTGGAGAAAGGAAGCTCAACAGGCCA  
CGGAGACACAGAGGAACGAGAAGTTCTGGCTCTCACGCTTGACTGCGGAGGAAAAGGAAGCC  
CCTTCCCAGGCCCCCTGAGGGGGACGTGATCTCGATGCCTCCCTCCACACATCTGAGGAGGA  
GCTGGGCTTCTCGAAGTTTGTCTCAGCGTAGGGCAGGAGGCCCTCCTGGCCAGGCCAGCAGT  
GAAGCAGTATGGCTGGCTGGATCAGCACCGATTCCCGAAAGCTTCCACCTCAGCCTCAGAG  
TCCAGCTGCCCCGACTCCAGGGCTCTCCCCACCCTCCCCAGGCTCTCCTCTTGATGTTCCA  
GCCTGACCTAGAAGCGTTTGTGAGCCCTGGAGCCCAGAGCGGTGGCCTTGCTCTTCCGGCTG  
GAGACTGGGACATCCCTGATAGGTTACATCCCTGGGCAGAGTACCAGGCTGCTGACCTCA  
GCAGGGCCAGACAAGGCTCAGTGGATCTGGTCTGAGTTTCAATCTGCCAGGAACCTCTGGGC  
CTCATGCCAGTGTGCGACCCCTGCCTTCTTCCCTCCACTCCAGACCCACCTTGTCTTCCCTCCC  
TGGCGTCTCAGACTTAGTCCCACGGTCTCCTGCATCAGCTGGTGATGAAGAGGAGCATGCT  
GGGGTGAGACTGGGATTCTGGCTTCTCTTTGAACCACCTGCATCCAGCCCTTCAGGAAGCCT  
GTGAAAAACGTGATTCTGGCCCCACCAAGACCCACCAAAACCATCTCTGGGCTTGGTGCAG  
GACTCTGAATTCTAACAATGCCAGTGACTGTGCGCACTTGAGTTTGAGGGCCAGTGGGCCTG  
ATGAACGCTCACACCCCTTCAGCTTAGAGTCTGCATTTGGGCTGTGACGTCTCCACCTGCCC  
CAATAGATCTGCTCTGTCTGCGACACCAGATCCACGTGGGGACTCCCCTGAGGCCTGCTAAG  
TCCAGGCCTTGGTCAGGTGAGTGCACATTGCAGGATAAGCCCAGGACCGGCACAGAAGTGG  
TTGCCTTTNCCATTTGCCCTCCCTGGNCCATGCCTTCTTGCCTTTGGAAAAAATGATGAAGA  
AAACCTTGGCTCCTTCCTTGTCTGGAAGGGTTACTTGCCTATGGGTTCTGGTGGCTAGAGA  
GAAAAGTAGAAAACCAGAGTGCACGTAGGTGTCTAACACAGAGGAGAGTAGGAACAGGGCGG  
ATACCTGAAGGTGACTCCGAGTCCAGCCCCCTGGAGAAGGGGTGCGGGGGTGGTGGTAAAGTA  
GCACAACTACTATTTTTTTTTCTTTTTCCATTATTATTGTTTTTTAAGACAGAATCTCGTGCT  
GCTGCCCAGGCTGGAGTGCAGTGGCACGATCTGCAAACTCCGCCTCCTGGGTTCAAGTGATT  
CTTCTGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGCACGCACCACCACACCTGGCTAATT  
TTTGTACTTTTAGTAGAGATGGGGTTTACCATTGTTGGCCAGGCTGGTCTTGAACCTCCTGAC  
CTCAAAATGAGCCTCCTGCTTCAGTCTCCCAAATTGCCGGGATTACAGGCATGAGCCACTGTG  
TCTGGCCCTATTTCCCTTTAAAAAGTGAAATTAAGAGTTGTTTCAAGTATGCAAACTTGGAAG  
ATGGAGGAGAAAAAGAAAAGGAAGAAAAAAATGTCACCCATAGTCTCACCAGAGACTATCAT  
TATTTTCGTTTTGTTGTACTTCCCTTCCACTCTTTTCTTCTTACATAATTTGCCGGTGTCTT  
TTTACAGAGCAATTATCTTGTATATACAACCTTTGTATCCTGCCTTTTCCACCTTATCGTTCC  
ATCACTTTATTCCAGCACTTCTCTGTGTTTACAGACCTTTTTTATAAATAAAATGTTTCATCA  
GCTGCATAAAAAAAAAAAAAA

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**FIGURE 330**

&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44196

&lt;subunit 1 of 1, 332 aa, 1 stop

&lt;MW: 36143, pI: 5.89, NX(S/T): 1

MRLLVLLWGCLLLPGYEALGPEEISGFEGD TVSLQCTYREELRDHRKYWCRKGGILFSRCS  
GTIYAEEEGQETMKGRVSIRDSRQELSLIVTLWNLT LQDAGEYWCGVEKRGPD ELLISLFV  
FPGPCCPPSPSPTTFQPLATTRLQPKAKAQQTQPPGLTSPGLYPAATTAKQGKTGAEAPPLPG  
TSQYGHERTSQYTGTSPHPATSPAGSSRPPMQLDSTSAEDTSPALSSGSSKPRVSIPMVRI  
LAPVLVLLSLLSAAGLIAFCSHLLLWRKEAQQATETQRNEKFWLSRLTAE EKEAPSQAPEGD  
VISMPPLHTSEEELGFSKFVSA

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domain:**

amino acids 248-269

**N-glycosylation site.**

amino acids 96-99

**Fibrinogen beta and gamma chains C-terminal domain.**

amino acids 104-113

**Ig like V-type domain:**

amino acids 13-128

# INTERNATIONAL SEARCH REPORT

National Application No  
PCT/US 00/08439

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K14/705 C12N15/62 C07K16/18  
G01N33/53 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | WO 98 39448 A (HUMAN GENOME SCIENCES INC)<br>11 September 1998 (1998-09-11)<br>see passages relating to gene 174 (clone H2MBF44) and the claims.<br>--- | 1-28                  |
| X          | WO 98 42741 A (GENETICS INST)<br>1 October 1998 (1998-10-01)<br>see passages relating to clone ck181_7 and the claims.<br>---                           | 1-28                  |
| A          | EP 0 834 563 A (SMITHKLINE BEECHAM CORP)<br>8 April 1998 (1998-04-08)<br>the whole document<br>---  |                       |
| A          | WO 97 07198 A (GENETICS INST)<br>27 February 1997 (1997-02-27)<br>the whole document<br>---   |                       |
|            | -/--  |                       |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 August 2000

Date of mailing of the international search report

13.11.00

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Authorized officer

Smalt, R

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No.    |
|------------|---|--------------------------|
| A          | YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator"<br>GENE,NL,ELSEVIER BIOMEDICAL PRESS.<br>AMSTERDAM,<br>vol. 163, no. 2,<br>3 October 1995 (1995-10-03), pages<br>193-196, XP004041983<br>ISSN: 0378-1119<br>the whole document<br>---     |                          |
| A          | KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors".<br>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON,<br>no. 93, 1 July 1996 (1996-07-01), pages<br>7108-7113, XP002077277<br>ISSN: 0027-8424<br>the whole document<br>--- |                          |
| P,X,<br>L  | WO 99 63088 A (BAKER KEVIN ;CHEN JIAN (US); GENENTECH INC (US); YUAN JEAN (US); G) 9 December 1999 (1999-12-09)<br>see passages relating to PRO281 and the claims. L: priority.<br>---  | 1-28                     |
| P,X        | WO 99 46375 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 16 September 1999 (1999-09-16)<br>see whole document, particularly passages relating to seq.ID'2 219 and 251<br>---  | 1-13,<br>17-28           |
| P,X        | WO 99 53040 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 21 October 1999 (1999-10-21)<br>page 1 -page 8<br>see claims.<br>page 128<br>---   | 1-13,<br>17-22,<br>24-28 |
| P,X        | WO 00 08145 A (NOVARTIS ERFINDUNGEN VERWALTUN ;NOVARTIS AG (CH); HOLNESS CLAIRE L) 17 February 2000 (2000-02-17)<br>the whole document<br>---   | 1-13,<br>21-28           |
| P,X        | WO 99 63083 A (TSURITANI KATSUKI ;ARASE SEIJI (JP); IKEDA AKIKO (JP); TAISHO PHAR) 9 December 1999 (1999-12-09)<br>abstract<br>see sequences.<br>-----  | 1-13,21,<br>22,25-28     |

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/08439

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-28, All partially.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-28, all partially

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0281 (seq.ID.2), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0281, chimeric protein comprising a portion corresponding to PR0281, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto.

2. Claims: Inventions 2-132: claims 1-28,  
all partially and claims 4 and 13 as far as  
applicable

Subject matter as defined for invention 1 above, but limited to the respective amino acid sequences and corresponding nucleic acid sequences referred to as:

2. PR0276 (seq.ID's 5/6),
3. PR0189 (Seq.ID's 7/8),
4. PR0190 (Seq.ID's 13/14),
5. PR0341 (Seq.ID's 19/20),
6. PR0180 (Seq.ID's 22/23),
7. PR0190 (Seq.ID's 13/14),
8. PR0194 (Seq.ID's 27/28),
9. PR0203 (Seq.ID's 29/30),
10. PR0290 (Seq.ID's 32/33),
11. PR0874 (Seq.ID's 35/36),
12. PR0710 (Seq.ID's 40/41),
13. PR01151 (Seq.ID's 46/47),
14. PR01281 (Seq.ID's 51/52),
15. PR0358 (Seq.ID's 56/57),
16. PR01310 (Seq.ID's 61/62),
17. PR0698 (Seq.ID's 66/67),
18. PR0732 (Seq.ID's 72/73),
19. PR01120 (Seq.ID's 83/84),
20. PR0537 (Seq.ID's 94/95),
21. PR0536 (Seq.ID's 96/97),
22. PR0535 (Seq.ID's 98/99),
23. PR0718 (Seq.ID's 102/103),
24. PR0872 (Seq.ID's 112/113),
25. PR01063 (Seq.ID's 114/115),
26. PR0619 (Seq.ID's 116/117),
27. PR01188 (Seq.ID's 123/124),
28. PR0784 (Seq.ID's 134/135),
29. PR0783 (Seq.ID's 137/138),
30. PR0820 (Seq.ID's 145/146),

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

31. PR01080 (Seq.ID's 147/148),
32. PR01079 (Seq.ID's 150/151),
33. PR0793 (Seq.ID's 152/153),
34. PR01016 (Seq.ID's 155/156),
35. PR01013 (Seq.ID's 157/158),
36. PR0937 (Seq.ID's 159/160),
37. PR0842 (Seq.ID's 164/165),
38. PR0839 (Seq.ID's 166/167),
39. PR01180 (Seq.ID's 168/169),
40. PR01134 (Seq.ID's 170/171),
41. PR0830 (Seq.ID's 174/175),
42. PR01115 (Seq.ID's 176/177),
43. PR01277 (Seq.ID's 178/179),
44. PR01135 (Seq.ID's 180/181),
45. PR0828 (Seq.ID's 188/189),
46. PR01009 (Seq.ID's 193/194),
47. PR01007 (Seq.ID's 196/197),
48. PR01056 (Seq.ID's 198/199),
49. PR0826 (Seq.ID's 200/201),
50. PR0819 (Seq.ID's 202/203),
51. PR01006 (Seq.ID's 204/205),
52. PR01112 (Seq.ID's 206/207),
53. PR01074 (Seq.ID's 208/209),
54. PR01005 (Seq.ID's 210/211),
55. PR01073 (Seq.ID's 212/213),
56. PR01152 (Seq.ID's 215/216),
57. PR01136 (Seq.ID's 218/219),
58. PR0813 (Seq.ID's 220/221),
59. PR0809 (Seq.ID's 222/223),
60. PR0791 (Seq.ID's 224/225),
61. PR01004 (Seq.ID's 226/227),
62. PR01111 (Seq.ID's 228/229),
63. PR01344 (Seq.ID's 230/231),
64. PR01109 (Seq.ID's 235/236),
65. PR01383 (Seq.ID's 240/241),
66. PR01003 (Seq.ID's 245/246),
67. PR01108 (Seq.ID's 247/248),
68. PR01137 (Seq.ID's 249/250),
69. PR01138 (Seq.ID's 252/253),
70. PR01054 (Seq.ID's 255/256),
71. PR0994 (Seq.ID's 257/258),

## 3. Claim : 1

72. PR0812 (Seq.ID's 259/260),
73. PR01069 (Seq.ID's 261/262),
74. PR01129 (Seq.ID's 263/264),
75. PR01068 (Seq.ID's 265/266),
76. PR01066 (Seq.ID's 267/268),
77. PR01184 (Seq.ID's 269/270),
78. PR01360 (Seq.ID's 271/272),
79. PR01029 (Seq.ID's 273/274),
80. PR01139 (Seq.ID's 275/276),
81. PR01309 (Seq.ID's 277/278),



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

82. PR01028 (Seq.ID's 280/281),
83. PR01027 (Seq.ID's 282/283),
84. PR01107 (Seq.ID's 284/285),
85. PR01140 (Seq.ID's 286/287),
86. PR01106 (Seq.ID's 288/289),
87. PR01291 (Seq.ID's 290/291),
88. PR01105 (Seq.ID's 292/293),
89. PR0511 (Seq.ID's 294/295),
90. PR01104 (Seq.ID's 296/297),
91. PR01100 (Seq.ID's 298/299),
92. PR0836 (Seq.ID's 300/301),
93. PR01141 (Seq.ID's 302/303),
94. PR01132 (Seq.ID's 308/309),
95. PR01346 (Seq.ID's 313/314),
96. PR01131 (Seq.ID's 318/319),
97. PR01281 (Seq.ID's 325/326),
98. PR01064 (Seq.ID's 333/334),
99. PR01379 (Seq.ID's 339/340),
100. PR0844 (Seq.ID's 344/345),
101. PR0848 (Seq.ID's 346/347),
102. PR01097 (Seq.ID's 348/349),
103. PR01153 (Seq.ID's 350/351),
104. PR01154 (Seq.ID's 352/353),
105. PR01182 (Seq.ID's 356/357),
106. PR01155 (Seq.ID's 358/359),
107. PR01156 (Seq.ID's 360/361),
108. PR01098 (Seq.ID's 362/363),
109. PR01127 (Seq.ID's 364/365),
110. PR01126 (Seq.ID's 366/367),
111. PR01125 (Seq.ID's 368/369),
112. PR01186 (Seq.ID's 370/371),
113. PR01198 (Seq.ID's 372/373),
114. PR01158 (Seq.ID's 374/375),
115. PR01159 (Seq.ID's 376/377),
116. PR01124 (Seq.ID's 378/379),
117. PR01287 (Seq.ID's 380/381),
118. PR01312 (Seq.ID's 386/387),
119. PR01192 (Seq.ID's 388/389),
120. PR01160 (Seq.ID's 393/394),
121. PR01187 (Seq.ID's 398/399),
122. PR01185 (Seq.ID's 400/401),
123. PR01345 (Seq.ID's 402/403),
124. PR01245 (Seq.ID's 407/408),
125. PR01358 (Seq.ID's 409/410),
126. PR01195 (Seq.ID's 411/412),
127. PR01270 (Seq.ID's 413/414),
128. PR01271 (Seq.ID's 415/416),
129. PR01375 (Seq.ID's 417/418),
130. PR01385 (Seq.ID's 419/420),
131. PR01384 (Seq.ID's 423/424),
132. PR09828 (Seq.ID's 510/511).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

4. Claims: Invention 133: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0943 (seq.ID.118), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0943, chimeric protein comprising a portion corresponding to PR0943, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa.

5. Claims: Inventions 134-136: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0183 (seq.ID.495), PR0184 (seq.ID.497) or PR0185 (seq.ID.499), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa, whereby invention 134 is limited to PR0183, invention 135 is limited to PR0184, and invention 136 is limited to PR0185.

6. Claims: Invention 137: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0331 (seq.ID.501), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0331, chimeric protein comprising a portion corresponding to PR0331, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

7. Claims: Invention 138: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01133 (seq.ID.129), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

8. Claims: Invention 139: claims 1-28,45-52,81-86,107-110,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01387 (seq.ID.422), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01387, chimeric protein comprising a portion corresponding to PR01387, antibody against said protein, the isolated extracellular domain of said protein or a protein with at

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa.

9. Claims: Invention 140 and 141: claims 1-28,45-52,81-86, 107-110,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0363 (seq.ID.503) or PR05723 (seq.ID.505), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa, whereby invention 140 is limited to PR0363 and invention 141 is limited to PR05723.

10. Claims: Invention 142: claims 1-28, 53-60,87-92,111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01114 (seq.ID.183), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01114, chimeric protein comprising a portion corresponding to PR01114, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa,

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa.

11. Claims: Invention 143 and 144: claims 1-28, 53-60, 87-92, 111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR03301 (seq.ID.507) or PR09940 (seq.ID.509), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa, and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa, whereby invention 143 is limited to PR03301 and invention 144 is limited to PR09940.

12. Claims: Invention 145: claims 1-28, 61-69, 93-98, 115-118,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01181 (seq.ID.355), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01181, chimeric protein comprising a portion corresponding to PR01181, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR07170, PR0361 or PR0846 through interaction with PR01181 and vice versa, method of linking a bioactive molecule to a cell expressing PR01181 using PR07170, PR0361 or PR0846 as binding ligands and vice versa, and method of modulating the activity of PR01181 by binding with PR07170, PR0361 or PR0846, and vice versa.

13. Claims: Inventions 146-148: claims 1-28, 61-69, 93-98,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

115-118,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO7170 (seq.ID.513), PRO361 (seq.ID.515) or PRO846 (seq.ID.517), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO7170, PRO361 or PRO846 through interaction with PRO1181 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1181 using PRO7170, PRO361 or PRO846 as binding ligands and vice versa, and method of modulating the activity of PRO1181 by binding with PRO7170, PRO361 or PRO846, and vice versa, whereby invention 146 is limited to PRO7170, invention 147 is limited to PRO361, and invention 148 is limited to PRO846.

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Information on patent family members

International Application No

PCT/US 00/08439

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